Impact of metastatic lymph nodes on survival in well and moderately differentiated appendiceal neuroendocrine tumors: whether current “lymph node-decided” surgical strategy benefits?

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Abstract

**Background** Current guidelines recommended right hemicolecctiony for appendiceal neuroendocrine tumors (A-NETs) patients with lymph node (LN) metastasis. Prognoses of these patients are favorable, and the prognostic impact of metastatic LN is controversial.

**Objective** The study aims to evaluate the prognostic factors of well and moderately differentiated A-NETs, and explore whether right hemicolecctiony/ more extended procedure (RHCM) improves prognosis compared to less extended than right hemicolecctiony (LRHC).

**Methods** The Fine-Gray proportional hazards model was established to calculate subdistribution hazard ratios of prognostic factors. A propensity score matching was performed to balance intergroup differences between the LRHC and RHCM groups. Survival difference between the after-matched groups was tested using the Gray test, and subgroup analyses were conducted.

**Results** In the multivariate analysis, age, race, histological type and distant metastatic status were associated with prognosis, while tumor size and nodal status were not. After propensity score matching, the patients’ characteristics were well balanced. RHCM did not confer survival advantage in the whole after-matched patients or any subgroup.

**Conclusions** Metastatic LN does not significantly impact prognosis, and RHCM fails to improve prognosis compared to LRHC. Therefore, the current “LN-decided” surgical procedure may not be suitable for patients with well and moderately differentiated A-NETs.

**Introduction**

Appendiceal neuroendocrine tumors (A-NETs) are rare, but they represent the most common tumor of the appendix, and their incidence has increased moderately in recent years[1-4]. Different from other neuroendocrine tumors, A-NETs are rarely accompanied with carcinoid syndrome, and their discovery are usually accidental after surgery for acute appendicitis, with around 0.5% of all appendectomies[5].

Some studies reported lymph node (LN) metastasis is a hallmark of aggressive behavior and a predictor for poor prognosis, while others reported favorable prognosis even in patients with metastatic LN and raised doubts about the prognostic value of metastatic LN[1, 6, 7]. However,
previous studies mostly included patients with both well and poor differentiated A-NETs, without considering different biological entities between these A-NETs [6, 8]. And it has been proved the well differentiated types are of indolent characteristic and favorable prognosis compared to the poor differentiated types[9, 10].

Oncological right hemicolecotomy is suggested for patients with LN metastasis or suspected LN metastasis, such as tumor size ≥ 2 cm, to eliminate tumor dissemination[1]. However, many studies now argue that this “LN-decided” surgical procedure failed to improve outcome[11-15]. Previous studies are mainly retrospective studies and case series. Considering the rarity and favorable prognosis of A-NETs, a randomized trial is difficult to conduct because of the enormous sample size and long follow-up period needed. Clinicians sometimes face dilemma that whether or not to perform a re-operation or an extended operation after initial appendectomy[11, 13].

Using a large, population-based database, our study focuses on well and moderately differentiated A-NETs. We aim to evaluate the prognostic factors, especially LN status, of well and moderately differentiated A-NETs, and explores whether right hemicolecotomy or extended surgery improves prognosis compared to less than right hemicolecotomy.

Methods

1. Data sources

The Surveillance, Epidemiology, and End Results (SEER) database collects information on cancer from registries sponsored by the US National Cancer Institution. In current, the SEER database consists of population-based cancer registries that cover 34.6% US population. The database collects data (e.g., patient demographics, primary tumor location, tumor morphology, diagnosis, and first course of treatment) and tracks the life status of patients.

The permission to access the database was obtained with reference number 14181-Nov2018. Our study was approved by the review board of the Jinhua Hospital of Zhejiang University School of Medicine. Patients with well and moderately differentiated A-NETs from 1988 to 2015 were identified by using the SEER Stat software. Patients diagnosed before 1988 were excluded because some variables were not collected on the database until 1998; patients diagnosed after 2015 were excluded
to ensure adequate follow-up period.

2. Inclusion and Exclusion Criteria

Patients met the following criteria were included: age of 18-80 years old; underwent curative-intend surgery (surgery of primary site codes 30-80); tumor site ICD-O-3 code 18.1 (appendix); histology ICD-O-3 codes 8240 (carcinoid tumor, malignant), 8241 (enterochromaffin cell carcinoid), 8242 (enterochromaffin-like cell tumor, malignant), 8244 (composite carcinoid), 8245 (adenocarcinoid tumor), 8246 (neuroendocrine carcinoma), 8249 (atypical carcinoid tumor). Goblet cell carcinoids were not included because it is now recognized to have a minor neuroendocrine component, and its classification changes to goblet cell adenocarcinoma in the 2019 WHO classification of tumors of the digestive system[16].

Patients met the following criteria were excluded: patients with incomplete documentation, such as tumor size and LN status, were excluded; patients with multiple primary tumors were excluded to eliminate the survival impact from other tumors; patients with survival time less than 1 month were excluded because these patients are at risk of death of perioperative complications.

3. Data collection

The age and year at diagnosis, gender, race, histological type, differentiation, tumor size, depth of invasion, status of LN and distant metastasis, surgical procedure, cause of death and survival months were retrieved from the SEER database. Race was classified into white, black and other. Histological type was classified into pure and mixed, and the former included malignant carcinoid tumor, enterochromaffin cell carcinoid, neuroendocrine cell carcinoma and the latter included composite carcinoid, adenocarcinoid tumor, atypical carcinoid tumor. Differentiation was classified into well and moderate differentiation. As previous studies reported, depth of invasion was obtained by combining the data of the collaborative stage and the extent of disease, resulting in three categories: invasion of the lamina propria (LP), invasion or through the muscularis propria (MP/TMP), or invasion through the serosa and adjacent structures (TS).[17]. LN status was categorized into no lymph nodes examined (NLNE), lymph nodes examined with negative lymph nodes (LNN) and lymph nodes examined with positive lymph nodes (LNP). According to “RX Summ - Surg Prim Site” values in the database, surgical
procedure was divided into two categories: right hemicolecctionomy/ more extended procedure (RHCM) and less extended than right hemicolecctionomy (LRHC).

4. Data analysis

Demographic and clinical characteristics of the cohort were reported as medians with interquartile ranges (IQR) for continuous variables, and frequency for categorical variables. Continuous variables were compared using Student t test or Mann-Whitney U test. Categorical variables were compared using chi-squared test or Fisher exact test.

The prognosis of patients with well and moderately differentiated A-NETs is favorable, and the incidence of non-cancer specific death (non-CSD) cannot be simply ignored when conducting a survival analysis[18]. Traditional Cox proportional hazard models only considered two statuses of outcome (e.g. alive and death), while competing risk models considered the presence of competing events (e.g. non-CSD). Thus, the competing risk model, rather than the Cox proportional hazard model, was applied in the study.

The time to cancer specific death (CSD) was calculated from the date of diagnosis to the date of death of cancer; the time to non-CSD was calculated from the date of diagnosis to the date of death of other causes. CSD was regarded as the outcome event, and non-CSD was regarded as the competing event. Univariate and multivariate analyses were conducted. In the univariate analyses, the cumulative incidences of CSD were calculated, and the differences were tested using the Gray tests. In the multivariate analyses, subdistribution hazard ratios (SHRs) were calculated to predict the association of variables with CSD (patients with tumor invasion of LP were excluded in both univariate and multivariate analyses because none of them dead of CSD)[19].

To reduce biases from confounders and achieve balance between the RHCM and LRHC groups, a propensity score matching was performed. Based on demographic and clinical characteristics (i.e., age, gender, race, histological type, differentiation, tumor size, depth of invasion, status of LN and distant metastasis), patients were matched with a 1:1 ratio using the nearest neighbor method (caliper set to 0.1)[20]. Absolute standardized differences were calculated to evaluate pre- and after-matched balance, and a “love plot” was plotted to present them[21]. The differences less than 10%
support intergroup balance, and 0% is considered no bias.

In the after-matched patients, the univariate analysis between the RHCM and LRHC groups was conducted to identify whether RHCM rendered a survival benefit compared to LRHC. In addition, subgroup analyses were conducted in these patients to explore whether RHCM improved outcomes in a certain group, and a “forest plot” was plotted to present the results.

The difference was considered to be statistically significant when the 2-side P-value was less than 0.05. R software (version 3.6) was applied for data analysis, and R packages survival, survminer, forestplot and cobalt were used.

Results

Patient characteristics

In total, 888 patients were identified from the SEER database, with 643 patients underwent LRHC and 245 patients underwent RHCM. In the LRHC group, over a half (68.27%) A-NETs were less than 10 mm, while only 9.80% were more than 20 mm; in the RHCM group, nearly a half (46.53%) A-NETs were more than 20 mm, while only 22.04% were less than 10 mm. Only 21.00% patients underwent lymphadenectomy when they were performed LRHC, and most of the retrieved LNs were negative. In comparison, most patients (91.84%) underwent lymphadenectomy in the RHCM group, and a third of the group (35.51%) had metastatic nodes (Table 1). In patients proved to have negative LNs, 42.34% (105/248) underwent right hemicolecotomy or extended surgery, while in patients proved to have metastatic LNs, 73.21% (82/112) underwent it.
### Table 1
Characteristics of patients in the LRHC group and RHCM group.

|                | LRHC     | RHCM     | P-value |
|----------------|----------|----------|---------|
| N              | 643      | 245      |         |
| Age (year, IQR)| 40 (27–53) | 48 (33–58) | < 0.01  |
| Sex            |          |          |         |
| Female (%)     | 381 (59.25) | 156 (63.67) | 0.26   |
| Male (%)       | 262 (40.75) | 89 (36.33)  |         |
| Race           |          |          |         |
| White (%)      | 562 (87.40) | 203 (82.86) | < 0.01  |
| Black (%)      | 48 (7.47) | 35 (14.29) |         |
| Other (%)      | 33 (5.13) | 7 (2.86)   |         |
| Pure (%)       | 594 (92.38) | 208 (84.90) | < 0.01  |
| Mixed (%)      | 49 (7.62) | 37 (15.10) |         |
| Differentiation|          |          |         |
| Well differentiation (%) | 534 (83.05) | 191 (77.96) | 0.10   |
| Moderate differentiation (%) | 109 (16.95) | 54 (22.04)  |         |
| Size (mm)      |          |          |         |
| ≤10 (%)        | 439 (68.27) | 54 (22.04)  | < 0.01  |
| 11–20 (%)      | 141 (21.93) | 77 (31.43)  |         |
| >21 (%)        | 63 (9.80) | 114 (46.53) |         |
| Depth of invasion|        |          |         |
| LP (%)         | 107 (16.64) | 14 (5.71)   | < 0.01  |
| MP/TMP (%)     | 446 (69.36) | 144 (58.78) |         |
| TS (%)         | 90 (14.00) | 87 (35.51)  |         |
| Nodal status   |          |          |         |
| NLNE (%)       | 508 (79.00) | 20 (8.16)   | < 0.01  |
| LNN (%)        | 105 (16.33) | 143 (58.37) |         |
| LNP (%)        | 30 (4.67)  | 82 (33.47)  |         |
| Metastatic status|       |          |         |
| No (%)         | 637 (99.07) | 234 (95.51) | < 0.01  |
| Yes (%)        | 6 (0.93)   | 11 (4.49)   |         |

Abbreviations: LRHC: less extended than right hemicolectomy; RHCM: right hemicolectomy/more extended procedure; LP: invasion of the lamina propria; MP/TMP: invasion or through the muscularis propria; TS: invasion through the serosa and adjacent structures; NLNE: no lymph nodes examined; LNN: lymph nodes examined with negative lymph nodes; LNP: lymph nodes examined with positive lymph nodes.

Intergroup differences indicated clinicopathological characteristics were not balanced between the two groups. In the RHCM group, A-NETs were poorer differentiation, higher invasion, and had higher proportion of LN or distant metastasis.

### Survival analysis

The endpoint date of follow-up was December 2016, and the median follow-up duration was 27 months (IQR: 17–45). In total, 15 patients (1.69%) and 14 patients (1.58%) suffered CSD and non-CSD, respectively (Fig. 1). Note that more patients suffered non-CSD than CSD (10 patients suffered non-CSD versus 7 patients suffered CSD) in the LRHC group.

At univariate analyses, age, race, histological type, differentiation, tumor size, depth of invasion, status of LN and distant metastasis were all significantly associated with CSD (Table 2). In patients underwent lymphadenectomy, the patients with LNP had significantly worse prognosis than those with LNN, and the 3-year CSD cumulative incidences was 4.72% in former while it was only 0.46% in latter
Patients in the LRHC and RHCM groups were matched 1:1, and there were 140 patients in each after-
matched group. Table 3 showed the demographic and clinical characteristics after matching, and P value of each variable was more than 0.05. Figure 2 showed the total absolute standardized difference was less than 10%, although the absolute standardized differences of some variables were more than 10%.

**Table 3**

| Characteristics of patients in the LRHC group and RHCM group after propensity score matching. | LRHC | RHCM | P-value |
|---|---|---|---|
| n | 140 | 140 | |
| Age (year, IQR) | 48 (31–55) | 47 (33–59) | 0.66 |
| Sex | | | |
| Female (%) | 85 (60.71) | 86 (61.43) | 1.00 |
| Male (%) | 55 (39.29) | 54 (38.57) | |
| Race | | | |
| White (%) | 118 (84.29) | 119 (85.00) | 0.89 |
| Black (%) | 18 (12.86) | 16 (11.43) | |
| Other (%) | 4 (2.86) | 5 (3.57) | |
| Histological type | | | |
| Pure (%) | 117 (83.57) | 116 (82.86) | 1.00 |
| Mixed (%) | 23 (16.43) | 24 (17.14) | |
| Differentiation | | | |
| Well differentiation (%) | 103 (73.57) | 103 (73.57) | 1.00 |
| Moderately differentiation (%) | 37 (26.43) | 37 (26.43) | |
| Size (mm) | | | |
| ≤10 (%) | 53 (37.86) | 50 (35.71) | 0.41 |
| 11–20 (%) | 48 (34.29) | 41 (29.29) | |
| >21 (%) | 39 (27.86) | 49 (35.00) | |
| Depth of invasion | | | |
| LP (%) | 17 (12.14) | 13 (9.29) | 0.73 |
| MP/TMP (%) | 81 (57.86) | 82 (58.57) | |
| TS (%) | 42 (30.00) | 45 (32.14) | |
| Nodal status | | | |
| NLNE (%) | 92 (65.71) | 83 (59.29) | 0.43 |
| LNN (%) | 28 (20.00) | 37 (26.43) | |
| LNP (%) | 20 (14.29) | 20 (14.29) | |
| Metastatic status | | | |
| No (%) | 136 (97.14) | 133 (95.00) | 0.54 |
| Yes (%) | 4 (2.86) | 7 (5.00) | |

Abbreviations: LRHC: less extended than right hemicolectomy; RHCM: right hemicolectomy/ more extended procedure; LP: invasion of the lamina propria; MP/TMP: invasion or through the muscularis propria; TS: invasion through the serosa and adjacent structures; NLNE: no lymph nodes examined; LNN: lymph nodes examined with negative lymph nodes; LNP: lymph nodes examined with positive lymph nodes.

**RHCM versus LRHC**

In the after-matched patients, the 3-year CSD cumulative incidences were 4.09% in the LRHC group and 1.84% in the RHCM group, and there was no significant difference between the two groups (P = 0.69). Results of subgroup analyses were also shown in the forest plot (Fig. 3), and none of the analyses showed significant difference of CSD cumulative incidences between the LRHC group and the RHCM group. Even in the subgroup analyses of patients with metastatic LN and tumor size > 20 mm, the RHCM group did not present a significantly better prognosis than the LRHC group.

**Discussions**
In the population-based study, we proved the prognosis of well and moderately differentiated A-NETs was extremely favorable, and the impact of non-CSD should be emphasized. In survival analysis, age, race, histological type and status of distant metastasis were associated with prognosis, while tumor size and LN status were not. Right hemicolecctomy or extended surgery failed to render survival benefit compared to less than right hemicolecctomy, even in the subgroup of patients with metastatic LN.

A-NETs are tumors of heterogeneous entities, and prognoses are various among different types[22]. Previous studies have shown that well and moderate A-NETs are of indolent clinical course and the prognosis of them is favorable, which was proved in our study with only 1.69% patients suffered CSD in the entire cohort. In addition, our study found non-CSD took a similar proportion as CSD. To our knowledge, there are only one study reported the impact of non-CSD in patients with appendiceal cancer[23]. The study of Jingjing Wu et al. focused on the entire appendiceal cancer and variables associated with non-CSD, while our study paid attention to the A-NETs and variables associated with CSD. Our results suggested non-CSD should be considered in clinical situations. For example, when making clinical decisions for patients who are old or accompanied with severe underlying diseases, appendectomy, rather than right hemicolecctomy, seems to be more suitable. It was also the reason why our study applied the competing risk model, rather than the Cox proportional hazard model, because the latter underestimates the cumulative incidences of CSD[24, 25].

Histological type is associated with prognosis and serves as an important predictor for survival[15]. Hsu C et al. compared characteristics and outcomes of malignant carcinoid tumor, goblet cell carcinoid and composite goblet cell carcinoid-adenocarcinoma from the American National Cancer Database, and found malignant carcinoid tumor had the best prognosis and composite goblet cell carcinoid-adenocarcinoma suffered the worst survival[22]. However, with deeper understanding of goblet cell carcinoid, it was classified to goblet cell adenocarcinoma in the 2019 WHO classification of tumors because of its minor neuroendocrine component[16]. Therefore, we excluded goblet cell adenocarcinoma in our study, and also confirmed the prognosis of pure A-NETs was much better than the mixed type.
Tumor size and LN status are regarded as main prognostic features of A-NETs. Tumor size $\geq$ 2 cm is the indication for right hemicolectomy in both the National Comprehensive Cancer Network (NCCN) and the ENETS guidelines because the risk of LN metastasis increases dramatically in $\geq$ 2 cm A-NETs[1]. However, neither the tumor size nor the nodal status was significantly associated with CSD when controlling confounders in our study, and some studies supported our findings. Rault-Petit et al. conducted a national study including 403 patients with nonmetastatic A-NETs, 26 of whom was surgically proved to have metastatic nodes, and only 1 patient had recurrence during the follow up[6]. Recently, Daskalakis et al. performed a meta-analysis including A-NETs patients, finding there was no significant difference in disease-specific survival between patients with and without lymph node metastasis (10-year disease-specific survival: 99.2% in patients without LN metastasis versus 95.6% in patients with LN metastasis)[26].

On the other hand, some previous studies are heterologous to our findings, and suggest metastatic LN is the predictor for poor outcome. Note that these previous studies included patients with poor differentiated A-NETs[27]. When focusing on patients with well differentiated A-NETs, some previous studies reported favorable prognosis even in LN metastasis patients. Lambert et al. reported 114 children and adolescents with well differentiated A-NETs, some of who had metastatic nodes (the exact number was not provided), and all patients were alive and disease free at the last follow up[7]. Combining results of our and previous studies, we concluded that metastatic LNs should not be regarded as a significant predictor for poor prognosis in patients with well and moderately differentiated A-NETs.

In 1987, Moertel et al. studied 150 patients with pure appendiceal carcinoid tumors, and found recurrences occurred very late and only happened to patients with $\geq$ 2 cm tumors[28]. Therefore, they suggested right hemicolecctomy was appropriate only for young patients with $\geq$ 2 cm tumors. As mentioned in the Background section, current guidelines for A-NETs were “LN-guided”. According to current guidelines, RHCM is routinely suggested for patients with LN metastasis or high probabilities of LN metastasis, such as vascular or lymph vessel invasion and mesoappendiceal infiltration $> 3$ mm, to eliminate metastatic lesions and achieve long-term survival. However, our study suggested RHCM
failed to render survival advantage compared to LRHC in both univariate and multivariate analyses. Our finding is supported by some results of previous studies. Crown et al. analyzed a multi-center cohort (61 patients) and found more radical surgical procedures, such as colon resection, did not improve long-term outcomes[11]. Bamboat et al. conducted a retrospective review of 48 A-NET patients, and they failed to find right hemicolectomy confers a prognostic benefit over appendectomy for tumors greater than 2.0 cm[29]. But, as far as we know, there has been no high-quality evidence comparing the prognostic benefits between LRHC and RHCM.

Considering the low incidence and long-term survival of A-NETs, it is difficult to conduct a randomized controlled trial to compare survival advantage between LRHC and RHCM. In our study, a propensity score matched analysis was performed to achieve intergroup balance, and surprisingly, we failed to observe survival advantage of RHCM over LRHC in the after-matched patients. Lukas Marti et al. hypothesized the reason for non-benefit of RHCM in appendiceal carcinoma was that LNs metastasis was limited, and ileocaecal resection was sufficient for removing metastatic LNs. But his hypothesis was based on LN metastatic patterns in colon cancer patients and need further confirmation, and we hypothesized that this non-benefit is “blamed” for the current “LN-decided” surgical strategy.

Current guidelines, as mentioned above, suggested performing RHCM for patients with LN metastasis or suspected LN metastasis, while in our study, LN metastasis was proved to be no associated with poor outcome in well and moderately differentiated A-NETs. And it indicated the current LN-decided surgical procedure was inappropriate. On the other hand, colon resection was reported to increase operation time, blood loss, complication rates and length of stay[11]. Reoperation also serves as an option for patients with local or distant recurrence during the follow-up period, and previous studies reported patients underwent reoperation could achieve long-term survival[7]. Thus, we concluded that LRHC, such as cecectomy, was curative for well and moderately differentiated A-NETs with LN metastasis, and MRHC did not improve prognosis.

Although our study is based on large population in the USA, it is also characterized by the following limitations. First, the SEER database does not contain records of vascular or lymph vessel invasion, margin states, Ki-67 index and mitotic rate, which may be associated with prognosis. Moreover, the
treatment records are incomplete and there is no detailed information regarding chemotherapy and radiotherapy, but A-NETs are considered to be non-sensitive to chemoradiotherapy. Also, the follow-up period is still too short considering the long-term survival in patients with well and moderately A-NETs. Finally, this study is a retrospective study and biases such as selection bias and treatment bias are inevitable in our study.

Conclusion

In conclusion, the study has demonstrated the prognosis of well and moderately differentiated A-NETs is extremely favorable, and non-CSD should be taken into consideration when making clinical decisions. Tumor size and LN status do not have significant impact on survival, and the current “LN-decided” surgical procedure is necessary to make changes in clinical practice because no survival advantage is found in RHCM compared to LRHC.

Clinical Practice Points

The prognosis of well and moderately differentiated A-NETs is extremely favorable, and non-cancer specific death should be taken into consideration when making clinical decisions Age, race, histological type and status of distant metastasis were associated with prognosis in the Fine-Gray proportional hazards model, while tumor size and LN status were not. In our study, 42.34% and 73.21% patients underwent right hemicolectomy or extended surgery in the negative lymph node group and positive lymph node group respectively, proving current guidelines are “LN-decided”. Right hemicolectomy or extended surgery failed to render survival benefits compared to less extended than right hemicolectomy, indicating current “LN-decided” surgical strategy is inappropriate.

Declarations

Acknowledgement:

None

Author contributions:

Haiping Lin: Study concept and design; collection, analysis, and interpretation of data; writing of the manuscript; and submission of the manuscript for publication. Liyuan Wang: Collection, analysis, and interpretation of data; writing of the manuscript. Yang Bai: Collection, analysis, and interpretation of data; writing of the manuscript. Shian Yu: Study concept and design; revision of the manuscript for important intellectual content; final approval for submission of the manuscript for publication.

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**Conflict of interest:**

None

**Ethical disclosure:**

We have obtained appropriate approval from institutional review board of the Jinhua Hospital of Zhejiang University School of Medicine

**Data sharing statement:**

The data used in the study are derived from a de-identified Surveillance, Epidemiology, and End Results (SEER) file (SEER ID: 14181-Nov2018). SEER is supported by the Surveillance Research Program (SRP) in NCI’s Division of Cancer Control and Population Sciences (DCCPS).

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Figures
Figure 1
Cumulative incidences of cancer specific death and non-cancer specific death.
Figure 2

“Love plot” that presents absolute standardized differences. Absolute standardized differences in baseline characteristics of LRHC group compared to RHCM group before and after 1:1 propensity score matching. Abbreviations: LRHC: less extended than right hemicolecstomy; RHCM: right hemicolecstomy/ more extended procedure; LP: invasion of the lamina propria; MP/TMP: invasion or through the muscularis propria; TS: invasion through the serosa and adjacent structures; NLNE: no lymph nodes examined; LNN: lymph nodes examined with negative lymph nodes; LNP: lymph nodes examined with positive lymph nodes.
Figure 3

“Forest plot” that presents the comparison of LRHC and RHCM in the whole after-matched patients and subgroups. a. Patients in those subgroups cannot be compared because no patient dead of cancer specific death in the LRHC or RHCM group, and the Gray test cannot performed in such situations. Abbreviations: LRHC: less extended than right hemicolecetomy; RHCM: right hemicolecetomy/ more extended procedure; LP: invasion of the lamina propria; MP/TMP: invasion or through the muscularis propria; TS: invasion through the serosa and adjacent structures; NLNE: no lymph nodes examined; LNN: lymph nodes examined with negative lymph nodes; LNP: lymph nodes examined with positive lymph nodes.