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REVIEW

Short- and long-term outcomes after transverse versus extended colectomy for transverse colon cancer. A systematic review and meta-analysis

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Abstract

Background Provide the surgeon with a tool to decide the best surgical approach to transverse colon cancer.
Objective To compare the surgical and oncological outcomes between transverse colectomy and extended hemicolectomy for patients with tumours of the transverse colon.
Data sources A systematic search was performed in the electronic databases (PubMed, Web of Science, Scopus, EMBASE), using the following search terms and/or MeSH terms in all possible combinations: transverse, transversus, colectomy, hemicolectomy, segmental resection, transverse colon cancer. The last search was performed on 10 May 2018.
Study selection Two independent authors (Mi.M. and N.V.) analysed each article and performed the data extraction independently. In case of disagreement, a third investigator was consulted (Ma.M.). Discrepancies were resolved by consensus.
Data extraction and synthesis Data regarding sample size, major clinical and demographic variables, oncologic outcomes and postoperative recovery and complications were extracted.
Main outcome measures Main outcomes analysed were anastomotic leakage, early mortality, hospital stay, operative time, overall complications rate, wound infection, harvested nodes and disease-free survival.
Results No statistical differences were found between transverse colectomy and extended hemicolectomy in short- and long-term outcomes; our results revealed no differences in disease-free survival between the two surgical approaches. As expected, a statistically significant difference was found in favour of extended hemicolectomy in terms of number of harvested lymph nodes.
Conclusions This systematic review with meta-analysis focus on the two major approaches to transverse colon cancer. The reviewed evidence suggests that a conservative approach to transverse colon cancer is feasible and safe and oncological outcomes are comparable between a conservative and an extended surgical procedure.

Keywords Transverse colectomy · Extended colectomy · Transverse colon cancer

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Introduction

Carcinoma of the transverse colon accounts for 10% of all colorectal cancer [1]. Tumours of the transverse colon have been less studied compared to other colorectal cancer and, because of the potential complexity and risk of complications, patients with transverse colon carcinoma have been excluded from large prospective randomised trials.

The best surgical approach is not already defined because it depends on the tumour location and extent of lymphatic spread. The completeness of resection requires a technically difficult lymph node dissection around the middle colic artery and a hard reconstruction of intestinal continuity [2]. The real 'gold standard' is still far to be defined and the dispute

between a conservative transverse colectomy (TC) and an aggressive extended hemicolectomy (HC) remains open. Nowadays, the surgeon choice is based on feasibility of a sufficient extended lymph node dissection and on a good survival results.

The aim of this systematic review with a meta-analysis is to explore literature to compare the surgical and oncological outcomes between TC and extended HC for patients with tumours of the transverse colon.

Materials and methods

A protocol for this review and meta-analysis was prospectively developed, detailing the specific objectives, the criteria for study selection, the approach to assess study quality, the outcomes and the statistical methods. All the studies comparing extended right/left hemicolectomy (HC) and transverse colectomy (TC) for transverse colon cancer were retrieved and included in the final analysis. No trial duration limitation was applied. Case reports, reviews, commentaries and conference abstract were excluded.

Using the Problem/Population, Intervention, Comparison and Outcome (PICO) framework, study selection criteria was exactly defined. Participants included adult population affected by histologically proven transverse colon cancer. Two types of interventions were included, extended right/left hemicolectomy and transverse segmental colectomy, with no limitation regarding the use of laparoscopy or other kind of minimally invasive surgery. No restrictions were placed about the fashion of anastomosis. In all included studies, we analysed short- and long-term outcomes after extended right/left hemicolectomy or transverse segmental colectomy. Primary outcome measure was anastomotic leakage, for the assessment of safety of procedures, and 5-year disease-free survival for the assessment of oncologic effectiveness. Secondary outcomes were divided in short- and long-term outcomes. Short-term outcomes consisted of operative time, number of harvested nodes, time to first flatus, length of hospital stay and postoperative complications (ileus, wound infection, mortality within 28 days, overall complications). Long-term outcomes were represented by incisional hernia and recurrence.

Literature search strategy

To identify all available studies, a detailed search was conducted according to Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines [3]. A systematic search was performed in the electronic databases (PubMed, Web of Science, Scopus, EMBASE), using the following search terms and/or MeSH terms in all possible combinations: transverse, transversus, colectomy, hemicolectomy, segmental resection, transverse colon cancer. The last search was performed on 10 May 2018. The search strategy included only English-speaking studies. In addition, the reference lists of all retrieved articles were manually reviewed. In case of missing data, study authors were contacted by e-mail to try to retrieve original data. In case of overlap between centres or authors, the most recent or with higher quality study was selected.

Study selection and quality assessment

Two independent authors (Mi.M. and N.V.) analysed each article and performed the data extraction independently. In case of disagreement, a third investigator was consulted (Ma.M.). Discrepancies were resolved by consensus. Selection results showed a high inter-reader agreement ($\kappa = 1$) and have been reported according to PRISMA flowchart (Appendix 1).

The evaluation of methodological quality of each study was performed with the Newcastle-Ottawa Scale (NOS), which is specifically developed to assess quality of non-randomised case-control studies [4]. The scoring system encompasses three major domains (selection, comparability, exposure) and a resulting score range between 0 and 8, a higher score representing a better methodological quality. Results of the NOS quality assessment are reported in Appendix 2.

Data extraction, statistical analysis and risk of bias assessment

Data regarding sample size, major clinical and demographic variables, oncologic outcomes and postoperative recovery and complications were extracted. Furthermore, long-term outcomes, i.e. incisional hernia, disease-free survival and recurrence were analysed.

Statistical analysis and risk of bias assessment was carried out using RevMan [Version 5.3, Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014].

Differences among cases and controls were expressed as mean difference (MD) with pertinent 95% confidence intervals (95% CI) for continuous variables and as odds ratio (OR) with pertinent 95% CI for dichotomous variables.

The overall effect was tested using Z scores and significance was set at $p < 0.05$. Statistical heterogeneity between studies was assessed with chi-square Cochran's Q test and with I^2 statistic, which measures the inconsistency across study results and describes the proportion of total variation in study estimates, which is due to heterogeneity rather than sampling error. In detail, I^2 values of 0% indicate no heterogeneity, 25% low, 25–50% moderate and 50% high heterogeneity [5].

Publication bias was assessed by Egger's test and represented graphically by funnel plots of the difference in means

versus the standard error. Visual inspection of funnel plot asymmetry was performed to address for possible small-study effect, and Egger's test was used to assess publication bias, over and above any subjective evaluation. A $p < 0.10$ was considered statistically significant [6]. In case of a significant publication bias, the Duval and Tweedie trim and fill method was used to allow for the estimation of an adjusted effect size [7].

In order to be as conservative as possible, the random-effect method was used for all analyses to take into account the variability among included studies.

Results

After excluding duplicates, the search identified 1123 articles. Of these studies, 1073 were excluded based on the title and/or abstract, 2 for language. No review or case report/case series was found. After full-text evaluation, other 43 articles were excluded: 41 were non-comparative studies, 2 for lack of data. Thus, five articles [8–12] comparing extended right/left hemicolectomy and transverse segmental colectomy were included in the final analysis. PRISMA flowchart for the study selection is shown in Appendix 1.

Studies characteristics

The included studies comparing extended right/left colectomy and transverse segmental colectomy for transverse colon cancer were 5, involving 11,687 patients, whereof 4664 cases (patients undergone transverse segmental colectomy) and 7023 controls (patients undergone extended right/left hemicolectomy) [8–12]. All studies were retrospective. Major characteristics of study populations are shown in Supplementary Table 1. The number of patients varied from 72 to 10,344, the mean age from 61 to 75.4 years and the prevalence of male gender from 38 to 60.5%. The mean body mass index (BMI) varied from 24 to 27.2 kg/m^2, even if it was reported by only two authors [8, 9]. The American Joint Committee on Cancer (AJCC) stage of the tumour was reported by four Authors [7–9, 12]. The prevalence of patients with AJCC tumoural stage I varied from 19 to 50%, with stage II from 29.4 to 55.3% and with stage III from 18.4 to 34.4%. No patients with stage IV tumour were included in the studies. Technical aspects of each surgical procedures were described by only two authors [9, 10], while van Rongen et al. [11] described only the transverse colectomy procedure. Matsuda et al. [9] compared only laparoscopic procedures, while Chong et al. [10] compared both open and laparoscopic techniques. The other articles did not express this aspect.

Primary outcomes

Primary outcomes are shown in Fig. 1. In details, anastomotic leakage was analysed by four authors [8–11], involving 1343 patients, 233 TC and 1110 HC, with no statistical difference between the two groups (OR = 1.15, $p = 0.83$, 95% CI 0.34, 3.86) and no statistically significant heterogeneity ($I^2 = 0\%$; $p = 0.72$).

A 5-year disease-free survival was reported by all authors, involving 11,687 patients, 4664 TC and 7023 HC, with no significant difference between the groups (OR = 1.05, $p = 0.28$, 95% CI 0.96, 1.13). Heterogeneity among these studies was not statistically significant ($I^2 = 0\%$; $p = 0.50$).

Short-term outcomes

Short-term outcomes are shown in Fig. 2. Operative time was analysed by three authors [8–10], involving 1240 patients (199 TC and 1041 HC), with no significant difference between the groups (MD = − 6.92, $p = 0.19$, 95% CI − 17.22, 3.39). Heterogeneity among the studies was no significant ($I^2 = 0\%$; $p = 0.70$).

Number of harvested nodes was reported by all authors. A statistically significant difference was found in favour of HC (MD = − 6.98, $p = < 0.00001$, 95% CI − 9.75, − 4.20), with a significant heterogeneity among the included articles ($I^2 = 100\%$; $p < 0.00001$).

Time to first flatus was analysed only by Matsuda et al. [9] and it was not possible to perform a meta-analysis.

Length of stay was analysed by only two authors [8, 9], involving 175 patients (72 TC and 103 HC); no significant difference was observed (MD = − 1.48, $p = 0.09$, 95% CI − 3.20, 0.23), with no significant heterogeneity among the studies ($I^2 = 50\%$; $p = 0.16$).

Postoperative complications

Postoperative complications are shown in Fig. 3. In details, postoperative ileus was reported by two authors [8, 10], involving 1168 patients (165 TC and 1003 HC). No significant difference was assessed (OR = 0.67, $p = 0.11$, 95% CI 0.41, 1.09), with no significant heterogeneity among the groups ($I^2 = 0\%$; $p = 0.80$).

Wound infection was analysed by three authors [8–10], involving 1240 patients (199 TC and 1041 HC), with no statistical difference between the groups (OR = 0.86, $p = 0.70$, 95% CI 0.41, 1.81) and no heterogeneity among the studies ($I^2 = 0\%$; $p = 0.50$).

Mortality within 28 days was reported by two authors [10, 11], involving 1168 patients (161 TC and 1007 HC). No statistically significant difference was assessed (OR = 1.02, $p = 0.98$, 95% CI 0.23, 4.57), with no heterogeneity among the studies ($I^2 = 0\%$; $p = 0.54$).

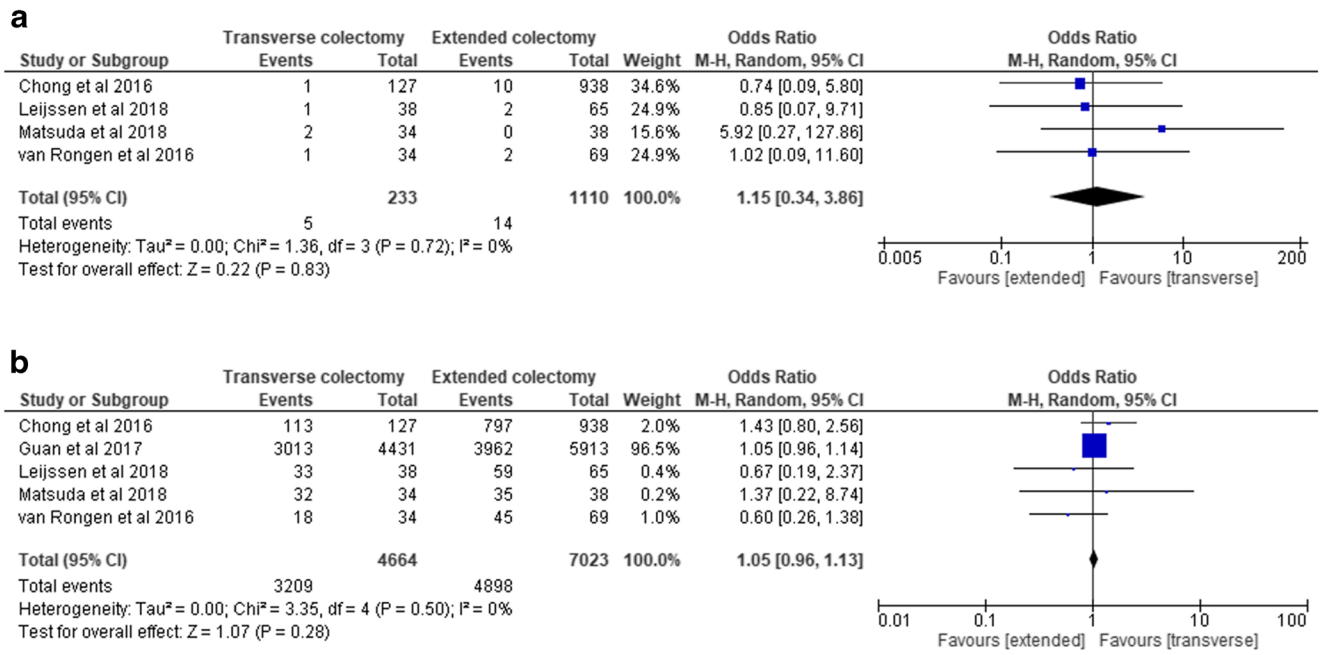

Fig. 1 Primary outcomes: **a** anastomotic leakage and **b** 5-year disease-free survival

The number of overall complications was reported by two authors [8, 9], involving 175 patients (72 TC and 103 HC), with no statistical difference between the groups (OR = 1.43, $p = 0.66$, 95% CI 0.28, 7.26). Statistically significant heterogeneity among the studies was found (I^2 = 79%; $p = 0.03$).

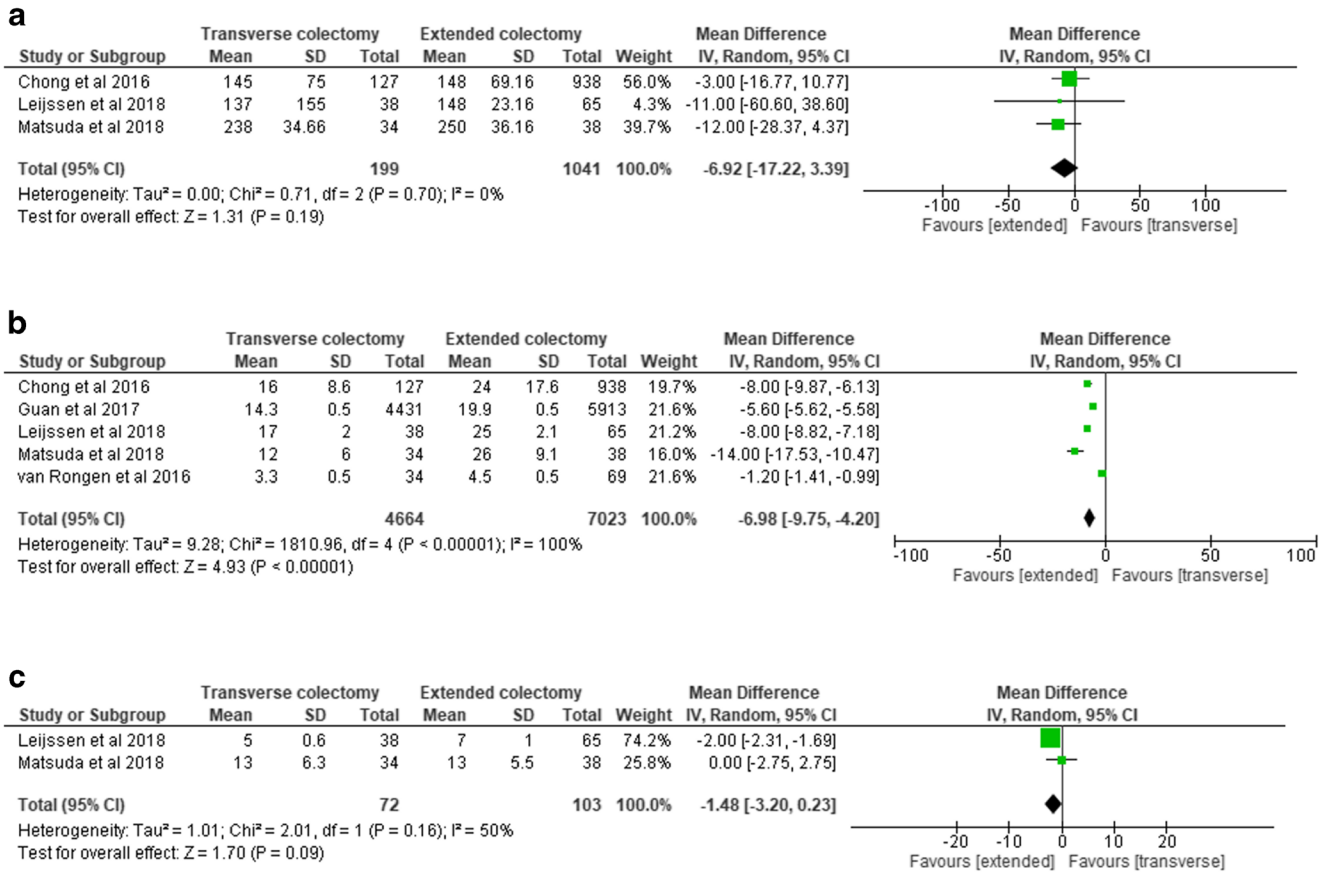

Fig. 2 Short-term outcomes: **a** operative time, **b** number of harvested nodes and **c** length of hospital stay

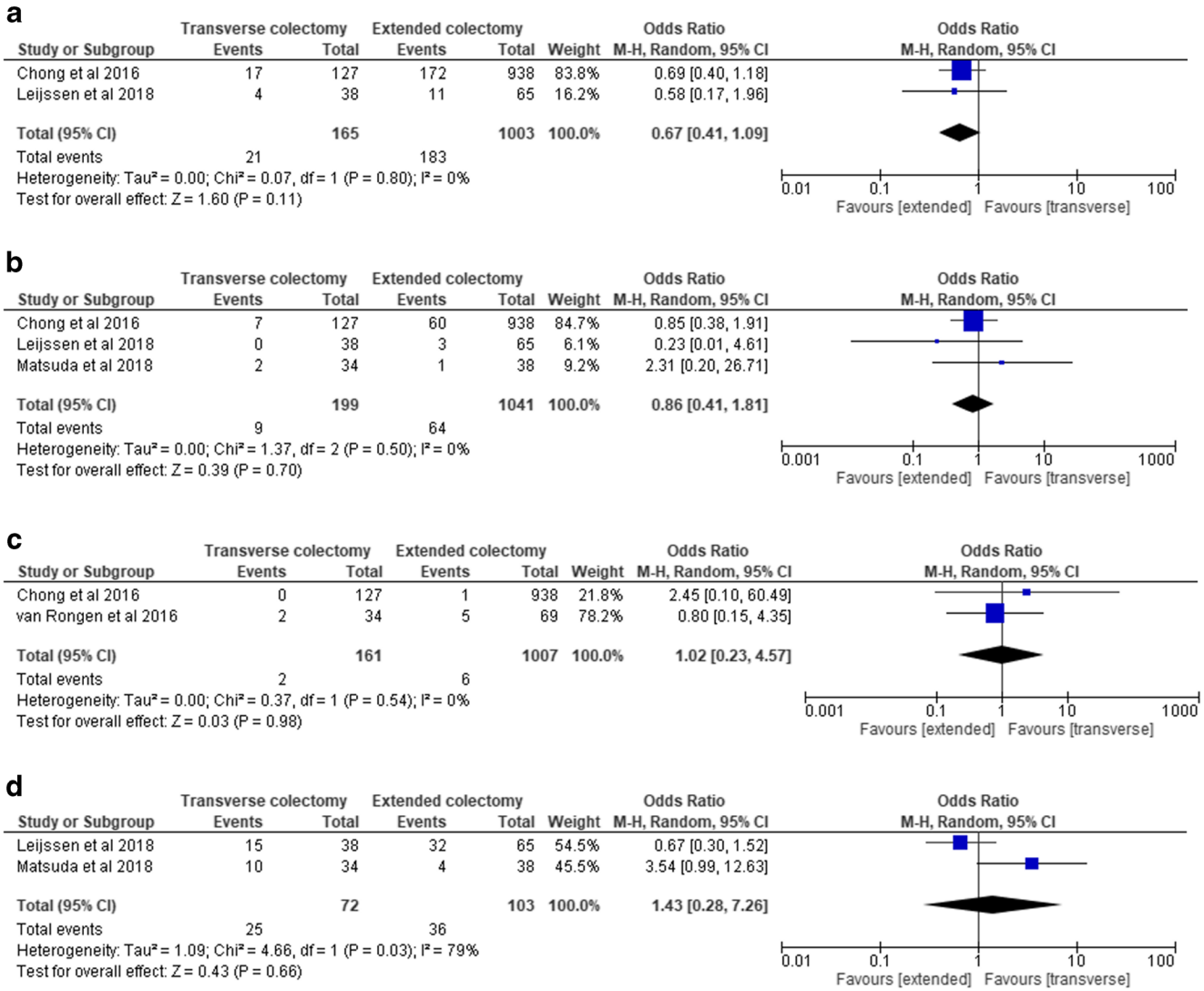

Fig. 3 Postoperative outcomes: **a** postoperative ileus, **b** wound infection, **c** mortality and **d** overall survival

Long-term outcomes

Long-term outcomes are shown in Fig. 4. Number of incisional hernia was reported only by Matsuda et al. [9]; thus, it was not possible to meta-analyse this data.

A 5-year recurrence was reported by two authors [8, 10], involving 1168 patients (165 TC and 1003 HC), with no statistically significant difference between the groups (OR = 0.78, $p = 0.38$, 95% CI 0.45, 1.35) and no heterogeneity among the studies ($I^2 = 0\%$; $p = 0.53$).

Publication bias

Because it is recognised that publication bias can affect the results of meta-analyses, we attempted to assess this potential bias using funnel plots analysis (shown in Supplementary Fig. 1). The distribution of studies evaluating operative time, harvested nodes, anastomotic leakage, wound infection and disease-free survival was symmetrical and no publication bias was found by Egger's test. It was not possible to perform a funnel plot analysis of hospital stay, postoperative ileus, mortality within 28 days, overall complications and recurrence because only two authors analysed this parameters.

Discussion

Transverse colon cancer has often been excluded in many prospective trials, and very few studies specifically investigated its long-term outcomes [13].

Although some studies have compared different techniques for transverse colon cancer, the optimal surgical approach remains unclear: some surgeons claim the safety and feasibility of less extensive procedures [14, 15] in contrast with supporters of a radical excision who sustains the necessity of an extended lymphadenectomy. Since knowledge is lacking

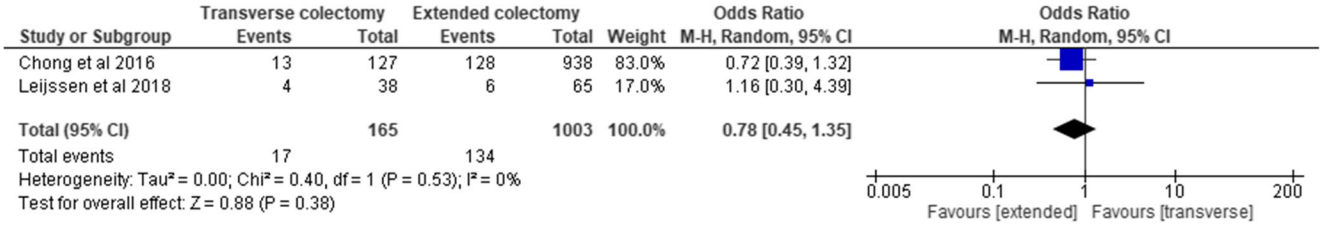

Fig. 4 Long-term outcome: 5-year recurrence

about the real surgical 'gold standard', the decision whether to perform an extended colectomy or a transverse colectomy is based on a surgeon's preference.

We have performed for the first time, in our best knowledge, a systematic review with meta-analysis focusing on the two major approaches to transverse colon cancer with the aim to give to surgeons an objective instrument of decision analysing the surgical and oncological outcomes of TC and HC.

Currently, few studies paid attention to the influence of surgical approaches on oncological outcomes among patients with transverse colon cancer who generally are not included in high quality trials; this resulted in a lack of evidence-based guidelines for this kind of procedures.

Among these few studies, Leijssen and colleagues [8] analysed differences between TC and HC on a total of 103 patients underwent elective and curative surgery for mid-transverse colon cancer; they underlined oncological safety of a transverse colectomy for stage I–III mid-transverse colon cancer with comparable postoperative morbidity between the two approaches. It is always clear that this study was limited by the small sample size, the not well-defined expertise of surgeon performing colectomy and the lack of randomisation of patients into the two analysed groups.

In 2013, van Rongen [11] and colleagues retrospectively analysed 103 patients with transverse colon cancer, founding no differences between TC and HC in terms of postoperative risk and, considering the satisfactory results found after partial transverse colectomy, they concluded that a segmental resection may be considered as an option for the treatment of localised tumours of the transverse colon. This study was limited by its plain research question, its retrospective design and the restricted use of preoperative diagnostic examinations because only in 21% of the patients the exact location of the tumour was known before surgery.

Matsuda et al. [9], in their retrospective study on 38 and 34 patients who received extended right hemicolectomy and transverse colectomy, respectively, concluded that both procedures provided similar oncological outcomes and an extended right hemicolectomy might be associated with fewer postoperative complications. Again, the number of the patients included in this study was small and we have also to consider that this was a retrospective study and patient selection bias cannot be excluded. Similar results were found by Chong et al. [10] on a large cohort of 1066 patients, of whom 750 underwent extended right hemicolectomy, 127 underwent transverse colectomy and 189 underwent left hemicolectomy; the researchers concluded that transverse colectomy and extended colectomy did not differ in terms of perioperative and oncological outcomes despite a shorter specimen length and fewer lymph nodes harvested in the transverse colectomy group.

The largest study realised to compare the oncological outcomes between PC and extended HC for patients with transverse colon cancer was made by Guan and colleagues [12]. Basing their results on a large-scale national cohort, authors found that, despite the less node examined by PC, the rate of node positivity was equal between PC and HC; moreover, they found that the 5-year cancer-specific survival for patients who underwent PC was similar to patients who received HC. The major limitation of this study was that authors identified the cancer cases from the Surveillance, Epidemiology, and End-Results (SEER) cancer registry which lack the information such as postoperative complications, surgical approach (laparoscopy surgery or open surgery) and short-term outcomes.

Our results involved 11,687 patients, of whom 4664 patients underwent transverse segmental colectomy and 7023 patients underwent extended hemicolectomy. As expected, no statistical differences were found between the two groups for main outcomes, as well as for postoperative complications, short-term and long-term outcomes. There was no difference in the anastomotic leakage between groups. The length of stay was analysed only in two studies and, again, no differences appeared between extended or selective surgical approach. It has to be underlined that no information could be extracted on the use of an enhanced recovery protocol (ERP) or on discharge criteria and this raised the potential risk for observational bias.

About short-term outcomes, the number of lymph nodes harvested with the specimen is often used as a surrogate marker of surgical quality: as expected, a statistically significant difference was found in favour of HC but nothing can be argued about this oncological outcome because selected researches failed to indicate the ratio between metastatic and examined lymph nodes (*N* ratio) [16] which is a simple and reproducible prognostic tool also in case of limited lymph node dissection. Moreover, a significant heterogeneity among the included articles was found because of the large differences in mean nodes harvested between surgeons (range 3–26) which could influence our results.

In relation to postoperative complications, our results demonstrated that the overall complication rate is not influenced by the chosen approach; by this point of view, no statistical differences were found in terms of wound infection and mortality within 28 days which were similar in patients underwent the two surgical techniques. About the oncological outcomes, our results shown that the 5-year disease-free survival and 5-year recurrence rate are similar for both PC and HC.

Conclusions

Overall, the reviewed evidence suggests that a conservative approach to transverse colon cancer is feasible and safe and, although transverse colon tumours are associated with poorer histopathological features, oncological outcomes are comparable between a conservative and an aggressive extended surgical procedure.

Our analysis is limited because of included studies did not have sufficient statistical power for the small sample size; moreover, no data can be extracted about technical aspects of each surgical procedures and no comparison can be made between laparoscopic and open approach.

Included studies do not describe the recovery of patients underwent PC and HC so nothing can be commented on this aspect. Furthermore, in our analysis only retrospective articles were included and this point out the possibility of patient selection bias.

Finally, the absence of a univocal pre-defined protocol for short- and long-term outcomes made us not able to conclude about the impact of surgical approach on this aspect of analysis results.

For a more definitive conclusion, prospective trials on a larger scale, with clear parameters of patient inclusion and a clear outcome definition, are required.

Author contributions Milone M: conception, design, interpretation of the data and drafting of the article; Manigrasso M, Elmore U, Rondelli F, Maione F, Velotti N: acquisition, analysis and interpretation of the data; De Palma GD: interpretation of the data and critical revisions; De Palma GD: critical revisions and final approval.

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