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Efficacy and safety of hybrid laparo-endoscopic surgery for colon tumors (systematic review and meta-analysis)

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ABSTRACT *AIM: to compare the efficacy and safety of hybrid laparo-endoscopic operations and laparoscopic segmental colectomy for benign endoscopically non-removable colorectal tumors.*
MATERIALS AND METHODS: systematic review and meta-analysis included 17 studies which evaluate the results of hybrid laparo-endoscopic procedure (main group) and laparoscopic segmental colectomy (control group). The study included 835 patients — 517 in main group and 318 controls.
RESULTS: operation time was significantly lower in main than in control group (mean difference = –38,7 minutes; 95% CI: –51,4 — –26, p < 0,00001). There was significant difference in postoperative hospital stay. It was shorter in main group (mean difference = –2,3 days; 95% CI: –3,17 — –1,57, p < 0,00001). There was not significant difference between odds ratio of postoperative morbidity (OR = 0,7; 95% CI: 0,38–1,53, p = 0,44), mortality (OR = 0,4; 95% CI: 0,07–3,11, p = 0,43) and local recurrence rate as well (OR = 2,8; 95% CI: 0,68–11,35, p = 0,15).
CONCLUSION: the hybrid laparo-endoscopic technique patients with benign endoscopically non-removable colon tumors does not increase the postoperative morbidity and mortality. At the same time, the hybrid technology reduces the operation time and postoperative hospital stay.

KEYWORDS: *hybrid operation, combined laparo-endoscopic surgery, laparoscopic resection of the colon, endoscopically unresectable adenomas, colon tumors*

CONFLICT OF INTEREST: *the authors declare no conflicts of interest*

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INTRODUCTION

Colorectal cancer continues to occupy one of the first places in the structure of cancer morbidity and mortality in developed countries [7,4]. In the vast majority of cases, malignant tumors of this locationoccurs from adenomatous polyps along the adenoma-carcinoma path [5,4]. It follows that effective prevention of colon cancer lies in the early detection and removal of colorectal tumors [22], while the standard of endoscopic treatment is their removal by mucosectomy (EMR — endoscopic mucosal resection) or dissection in the submucosal layer (ESD — endoscopic submucosal dissection). According to the literature, 10–15% of all colorectal polyps cannot be removed endoscopically [10,26,38]. The reasons for this are factors such as the large size of the tumor, location at the ostium of the diverticulum or appendix, as well as the presence of fibrous changes in the submucosal layer of the intestinal wall [9,25,30,37]. Previously, in such cases, patients undergo resection of a segment of the colon, which is associated with a higher risk of complications, with incidence of 18% [29]. It is also necessary to take into account the fact that the majority of endoscopically

unremovable tumors turn out to be benign according to the results of pathomorphology, and adenocarcinoma is detected only in 18–34% of cases [3,32].

Recently, thanks to advances in imaging technology and minimally invasive interventions, combined or hybrid laparoscopic-endoscopic interventions are being actively introduced into clinical practice.

It should be emphasized that most of the studies devoted to the study of the safety and effectiveness of this technology in colorectal surgery are represented by studies with a low evidence base. Another factor complicating the analysis of literature data is the lack of standardization of the implementation of this type of procedure. A literature search found only one randomized trial comparing the results of hybrid laparo-endoscopic operations and laparoscopic colon resections, but it had a small sample of patients [19].

Taking into account the above circumstances, it was decided to make a systematic literature review and meta-analysis, the purpose of which is to compare the effectiveness and safety of hybrid laparo-endoscopic operations and laparoscopic segmental resections in patients with colon tumors without signs of invasive growth and not subject to endoscopic removal.

MATERIALS AND METHODS

The systematic review and meta-analysis were performed in accordance with the recommendations of the preferred reporting items for systematic reviews and meta-analysis checklist (PRISMA) [23]. The search for publications was carried out in electronic medical literature databases Medline and finished by December 2022. The selection was performed using the following keywords and phrases: “laparoscopy assisted”, “endoscopy”, “polypectomy”, “laparo-endoscopic resection”, “full-thickness excision” and “laparoscopic resection” using the suffixes [OR] and [AND]. Studies on children and animals were excluded from the query using appropriate filters, and no language restrictions were applied. Additionally, a search of sources was carried out using the bibliographic lists of selected articles in order to include in the meta-analysis publications that were not found during the initial search.

Criteria for selecting publications for inclusion in the review

Criteria for inclusion in the analysis: comparison of the incidence and structure of perioperative morbidity and treatment results after hybrid laparo-endoscopic interventions and laparoscopic segmental resections of the colon.

The review did not include publications that compared the results of the use of hybrid laparo-endoscopic operations with open resections of the colon, and with endoscopic methods, such as endoscopic full-thickness resection (EFTR — endoscopic full-thickness resection using a special device) in the treatment of benign colorectal neoplasms.

Statistical analysis

Statistical processing of data when comparing the above treatment methods was performed in the Review Manager 5.4 program. The summary value of dichotomous data was described with a 95% confidence interval (CI) as an odds ratio (OR). Statistical heterogeneity among studies included in the meta-analysis was assessed using the χ^2 test. When $p < 0.1$ and I2 > 50%, heterogeneity was considered statistically significant.

Results of the search

After composing a query in the PubMed system, 3402 literature sources were found in the Medline database. An additional search of the bibliographic data of the selected articles revealed 1 additional paper. Further screening of publications excluded 3341 articles where there was no comparative analysis of the use of two methods, leaving 62 full-text publications. At the next stage, literature reviews, meta-analyses and studies comparing with other methods of treatment of patients with benign neoplasms of the colon that were not endoscopically resectable, namely: open resection of a segment of the colon, polypectomy through colotomy, EFTR, were excluded.

Ultimately, seventeen clinical studies were included in the analysis (Fig. 1).

Receiving data

The data of interest included in the analysis were as follows: author, year of publication, study design, follow-up period, number of patients in the compared groups, site and size of the tumor, surgical technique, operation time, structure and rate of intra- and postoperative complications, re-operations rate, hospital stay, morphology of the removed specimen, as well as the recurrence rate.

Quality of articles

The quality of a randomized study was assessed in accordance with the Cochrane risk of bias check list [14], non-randomized studies — using the Newcastle-Ottawa scale (NOS). The maximum value of the sum of points for each study is 9. At a level of 8–9 points, the study has a low risk of systematic errors. Of the 17 publications that met the inclusion criteria, there was 1 prospective randomized [19], 7 prospective non-randomized [1,6,8,12,20,34,35] and 9 retrospective studies [11,13,16,17,24,28,31,33,36]. The results of treatment of 517 patients in the group of hybrid operations and 318 patients in the group of laparoscopic colon resections were analyzed. Characteristics of publications are presented in Table 1.

It should be noted that only 3 publications had a low risk of bias in studies assessed according to the Newcastle-Ottawa Scale (NOS) [11,30,36].

Homogeneity of groups

Data on the gender of patients in the compared groups are provided in 7 of the 17 studies included in the analysis (Fig. 2). When comparing groups for this parameter, no statistically significant differences were obtained (OR = 1.1; 95% CI 0.66–1.90; $p = 0.69$).

Information on the age of patients in both groups was correctly reflected in 2 of 17 studies (Fig. 3). From the data presented, we can conclude that the compared groups were comparable in age (Mean difference = –5.3; 95% CI –11.07–0.5; $p = 0.07$).

Nine out of 17 studies included in the analysis (Fig. 4): there were no significant differences in the groups of hybrid laparo-endoscopic interventions and laparoscopic resections for right colon tumors (OR = 0.5; 95% CI 0.28–0.99; $p = 0.05$).

Data on tumor site in the left colon are extracted from 7 of 17 studies included in the meta-analysis

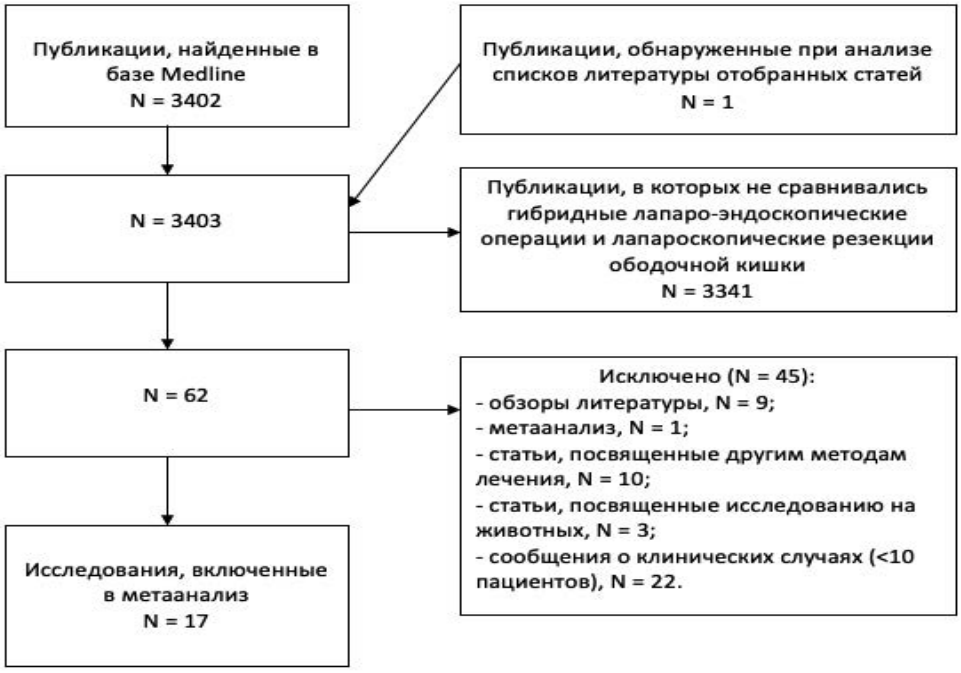

Figure 1. *Block diagram of inclusion of literature sources*

Table 1. *Characteristics of the studies included in the meta-analysis*

Автор	Год	Страна	Срок наблюдения (мес.)	Дизайн исследования	Шкала оценки качества по NOS	Метод операции	N пациентов	Пол, М / Ж	Размер образования (см)	Рецидивы, N
Winter et al.	2007	Германия	54	Проспективное	6	Гибрид	8	5/3	н/д	0
						Резекция	38	15/15	н/д	0
Franklin et al.	2009	США	65	Проспективное	7	Гибрид	154	н/д	н/д	0
						Резекция	22	н/д	н/д	0
* Lascarides et al.	2016	США	15,3	Проспективное	-	Гибрид	17	9/8	2 (1-5)	1
						Резекция	17	11/6	2 (1-5)	0
Lee et al.	2013	США	65	Проспективное	4	Гибрид	48	н/д	н/д	5
						Резекция	27	н/д	н/д	н/д
Grunhagen et al.	2011	Нидерланды	11	Проспективное	7	Гибрид	9	6/3	н/д	0
						Резекция	2	1/1	н/д	0
Agrawal et al.	2010	США	3	Проспективное	7	Гибрид	11	5/6	0,8-4	0
						Резекция	7	2/5	3,7 (0,6-6)	0
Ommer et al.	2003	Германия	нд	Ретроспективное	5	Гибрид	17	н/д	н/д	н/д
						Резекция	4	н/д	н/д	н/д
Wilhelm et al.	2009	Германия	35	Ретроспективное	7	Гибрид	120	н/д	н/д	н/д
						Резекция	26	н/д	н/д	н/д
Wood et al.	2011	Англия	нд	Проспективное	5	Гибрид	10	н/д	н/д	н/д
						Резекция	3	н/д	н/д	н/д
Yan et al.	2011	США	12	Ретроспективное	8	Гибрид	20	н/д	н/д	3
						Резекция	3	н/д	н/д	0
Jang et al .	2012	США	3	Ретроспективное	5	Гибрид	17	н/д	н/д	2
						Резекция	9	н/д	н/д	0
Goh et al.	2013	Ирландия	19,8	Ретроспективное	8	Гибрид	22	н/д	н/д	0
						Резекция	8	н/д	н/д	0
Cruz et al.	2011	США	нд	Ретроспективное	6	Гибрид	25	13/12	2,4 ± 0,9 (1-4)	н/д
						Резекция	68	35/33	2,9 ± 1,2 (1-8)	н/д
Currie et al.	2019	Англия	нд	Проспективное	5	Гибрид	8	н/д	н/д	н/д
						Резекция	3	н/д	4 (3,5-4,3)	н/д
Suzuki et al.	2019	Япония	32	Ретроспективное	8	Гибрид	15	10/5	2 (0,5–3,3)	0
						Резекция	68	39/29	3,4 (0,6–9)	1
Porfidia et al.	2017	Италия	12	Ретроспективное	6	Гибрид	6	н/д	н/д	0
						Резекция	9	н/д	н/д	0
Jayaram et al.	2018	США	нд	Ретроспективное	7	Гибрид	10	5/5	2.8 ± 0.91	н/д
						Резекция	12	7/5	2.8 ± 1.5	н/д

* - РКИ

(Fig. 5). When comparing groups for this parameter, no statistically significant differences were obtained (OR = 1.9; 95% CI 0.89–4.3; $p = 0.09$).

Information on tumor site in the transverse colon extracted from 7 of 17 studies (Fig. 6). The compared groups were also comparable in this parameter (OR = 1.6; 95% CI 0.69–3.86; $p = 0.27$).

RESULTS

The operative time was assessed in 5 studies (Fig. 7). It turned out to be statistically significantly less in the group of hybrid laparo-endoscopic operations, compared with laparoscopic segmental resections of the colon (Mean difference = –38.7 minutes; 95% CI –51.40 — –26.02; $p < 0.00001$).

An analysis of the postoperative morbidity was carried out in 14 studies (Fig. 8). The incidence of postoperative complications in the main group was 10.3% (23 patients), in the control group — 9.7% (26 patients). The likelihood of complications did not differ statistically significantly between the groups (OR = 0.7; 95% CI 0.38–1.53; $p = 0.44$).

We also assessed the rate and likelihood of developing life-threatening complications such as anastomotic leakage and intestinal bleeding.

Analysis of the complications structure was presented in 10 of 17 studies. No anastomotic leakage was found in the group of hybrid laparo-endoscopic interventions, but in the group of laparoscopic colon resections it developed in 9 (3.7%) patients. The likelihood of anastomotic leakage (Fig. 9) did not differ statistically significantly (OR = 0.3; 95% CI 0.09–1.14; $p = 0.08$).

The incidence of intestinal bleeding in the group of hybrid interventions was 1.8% (3 patients), in the group of laparoscopic resections — 0.4% (1 patient). There were no statistically significant differences in the compared groups in the likelihood of this complication (OR = 1.0; 95% CI 0.20–5.66; $p = 0.94$) (Fig. 10).

Data on the reoperations rate were presented in 8 of 17 studies (Fig. 11). In the main group it was

4% (4 patients), in the control group — 4.05% (6 patients). When comparing groups in terms of the likelihood of reoperations, no statistically significant differences were found (OR = 0.7; 95% CI 0.23–2.38; $p = 0.62$).

Information on 30-day mortality was provided in 17 studies (Fig. 12). In the hybrid group, the death of one (0.19%) of 517 patients was reported as a result of acute myocardial infarction in the postoperative period. In the resection group, there were two (0.62%) deaths out

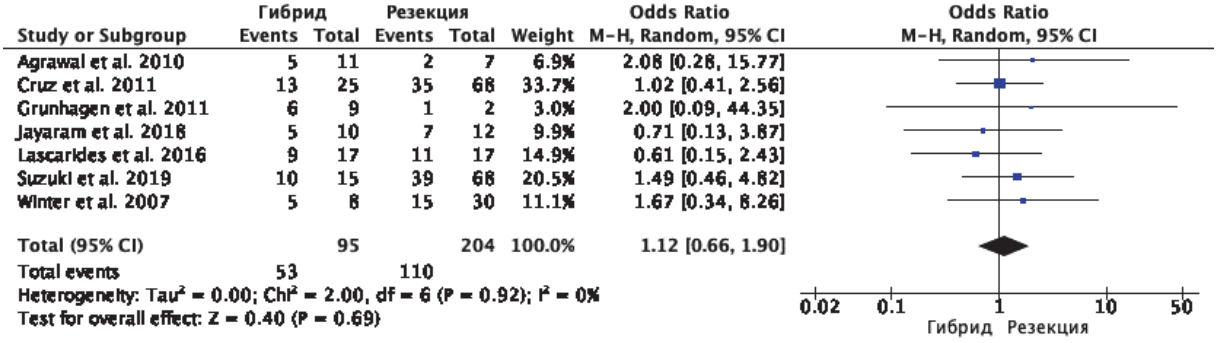

Figure 2. *Gender of patients in groups*

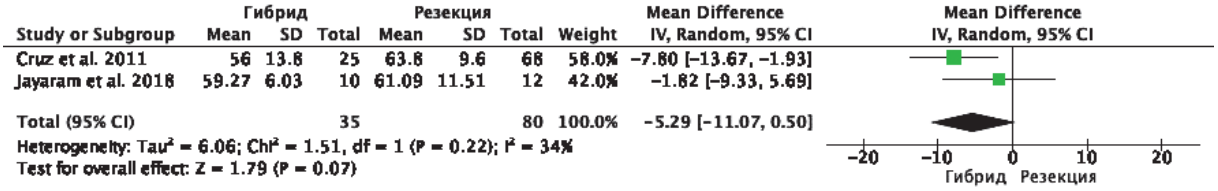

Figure 3. *Age of patients in groups*

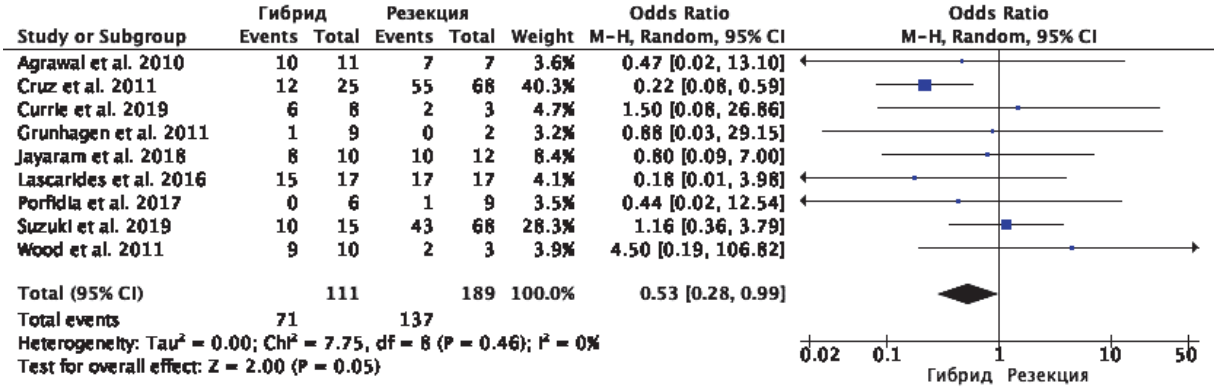

Figure 4. *Localization of neoplasms in the right parts of the colon in groups*

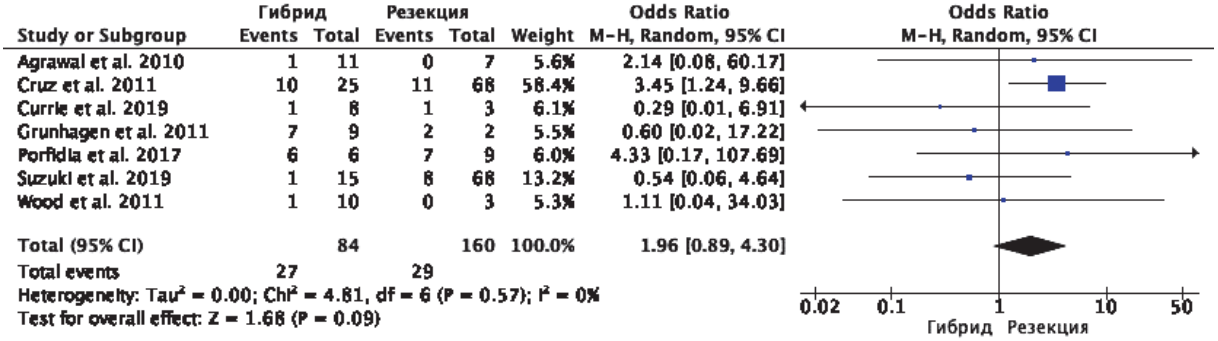

Figure 5. *Localization of neoplasms in the left colon in groups*

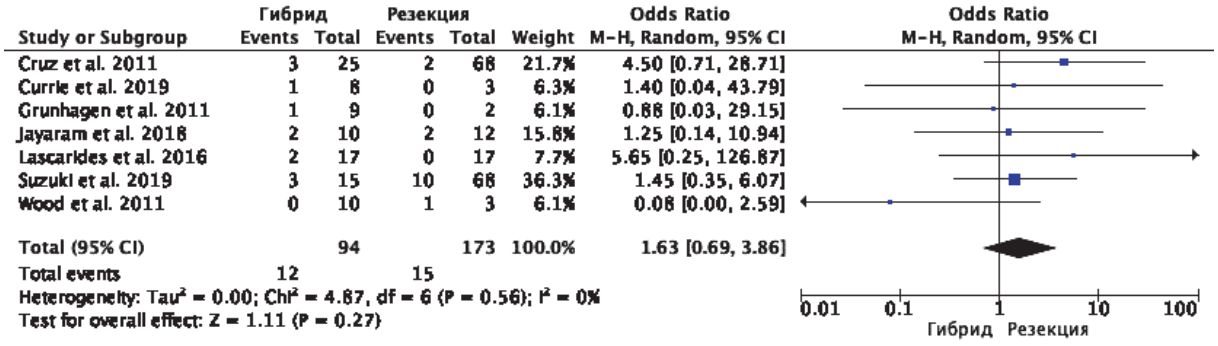

Figure 6. *Localization of neoplasms in the transverse colon in groups*

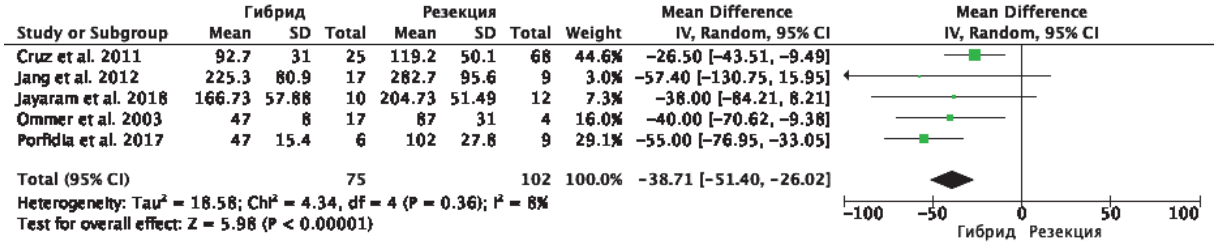

Figure 7. *Duration of the operation in groups*

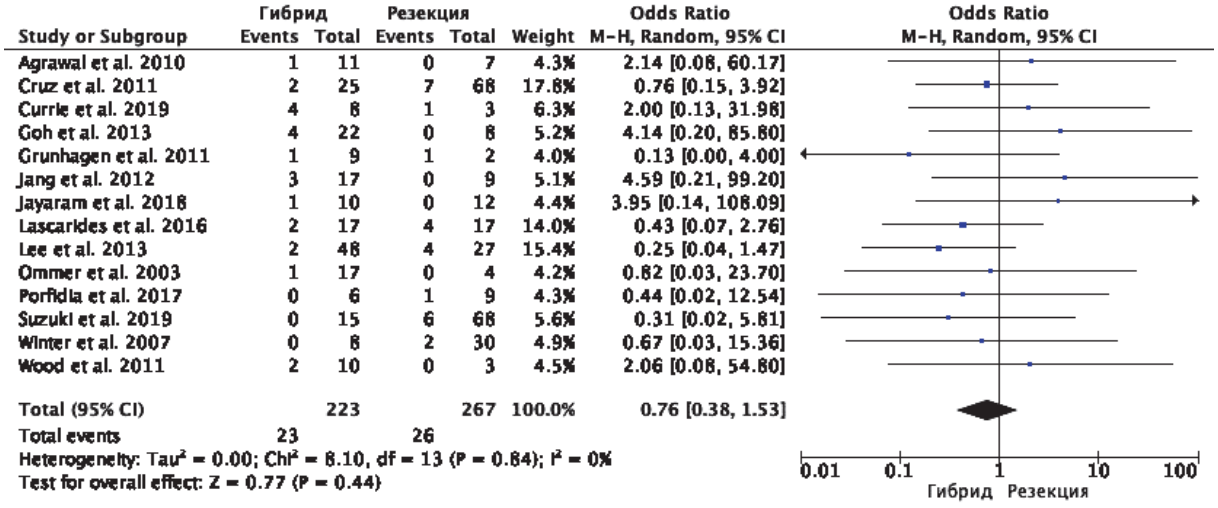

Figure 8. *Probability of postoperative complications in groups*

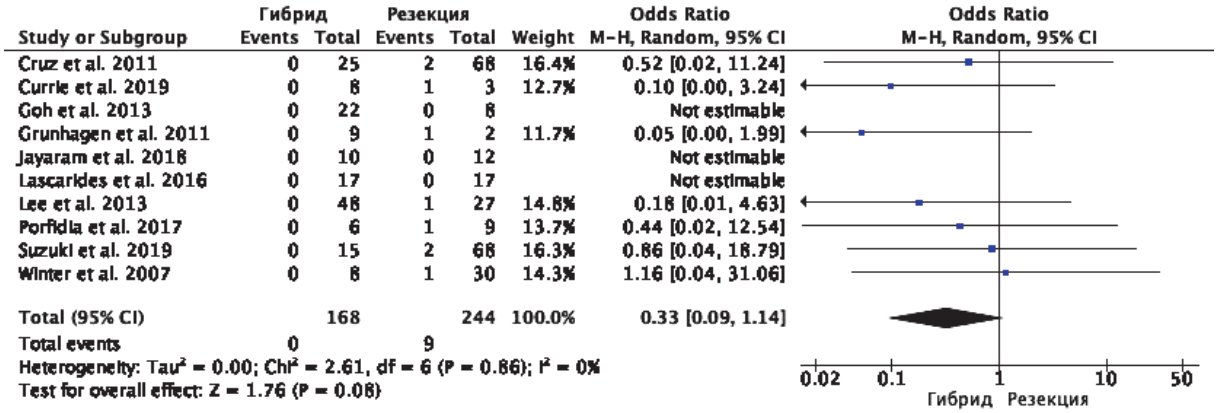

Figure 9. *Probability of intestinal anastomosis failure in groups*

of 318 patients: one was due to progression of the oncological process (at the time of surgery, the patient showed multiple metastatic liver lesions), the cause of the second death was peritonitis and multiple organ failure, as a result of anastomosis leakage. When comparing the probability of death in the early postoperative period, there were no statistically significant differences between the groups (OR = 0.4; 95% CI 0.07–3.11; $p = 0.43$).

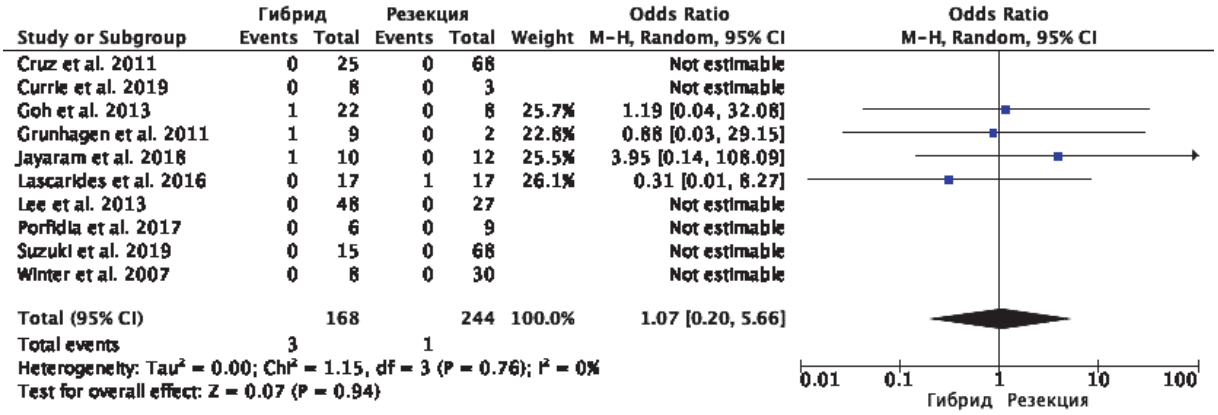

Figure 10. *The probability of intestinal bleeding in groups*

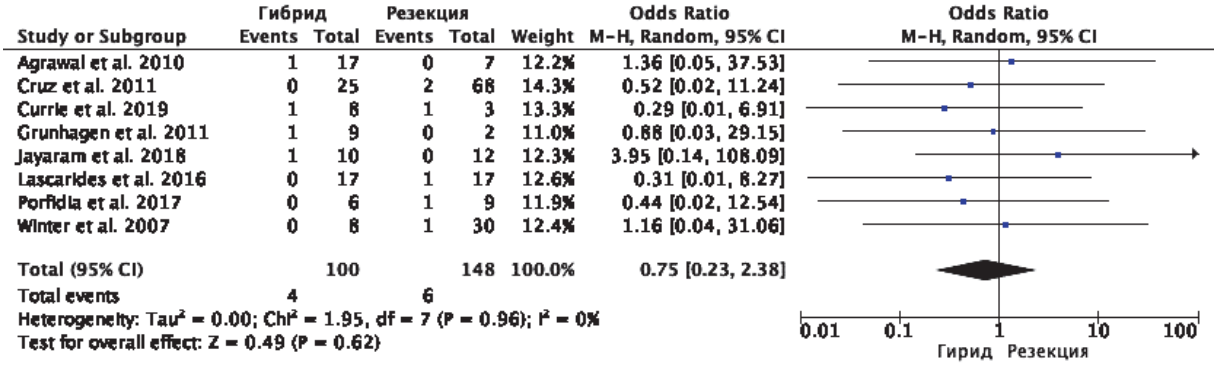

Figure 11. *The probability of performing repeated operations for the developed complications in the groups*

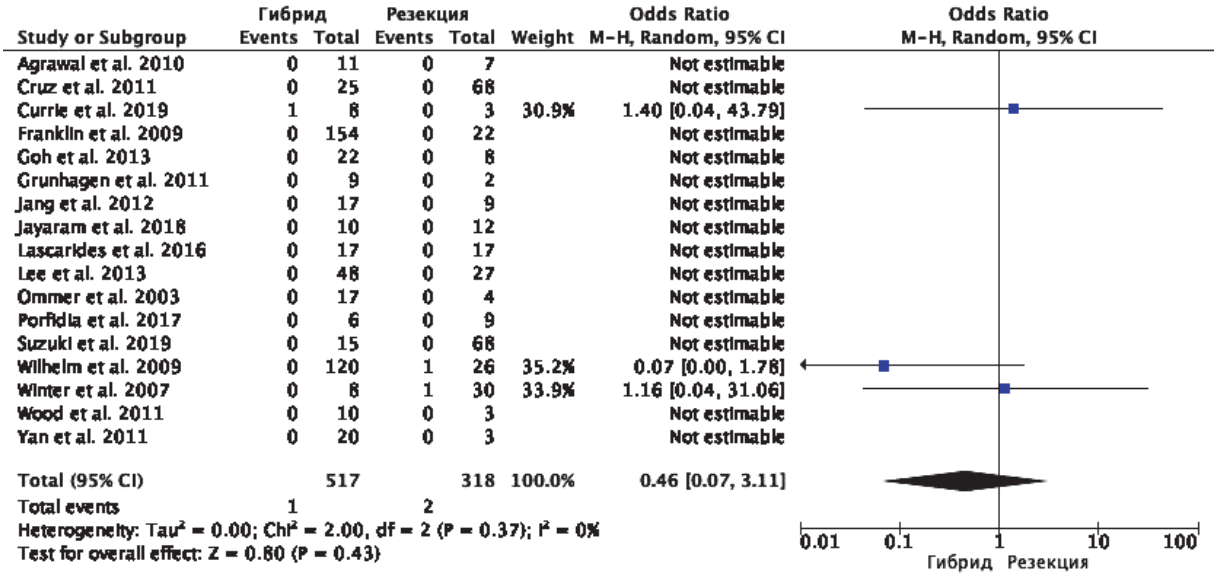

Figure 12. *Probability of 30-day mortality in groups*

The postoperative hospital stay reported in 2 studies (Fig. 13) was reduced by more than 2 days after hybrid surgery compared with the laparoscopic resection group (Mean difference = –2.3 days; 95% CI –3.17 — –1.57; $p < 0.00001$).

Data from the pathology of the removed specimens were presented in 15 studies included in the analysis (Fig. 14). Adenocarcinoma was detected in 23 (6.1%) of 377 cases in the main group, and in 103 (35.6%) of 289 cases in the control group. The probability of detecting adenocarcinoma was statistically significantly higher in the group of laparoscopic segmental resections of the colon, compared with the group of hybrid operations (OR = 0.3; 95% CI 0.10–0.87; $p = 0.03$).

Information on the reoperations rate for oncological indications after hybrid laparo-endoscopic operations is presented in 8 studies. Radical surgery was required in 19 (8.3%) of 227 patients.

The incidence of local recurrence was assessed in 5 of 17 studies (Fig. 15). In the main group, local relapse was detected in 11 (9.4%) patients, in the control group — in 1 (0.8%) patient. When analyzing the probability of local recurrence, no statistically significant differences were obtained (OR = 2.8; 95% CI 0.68–11.35; $p = 0.15$).

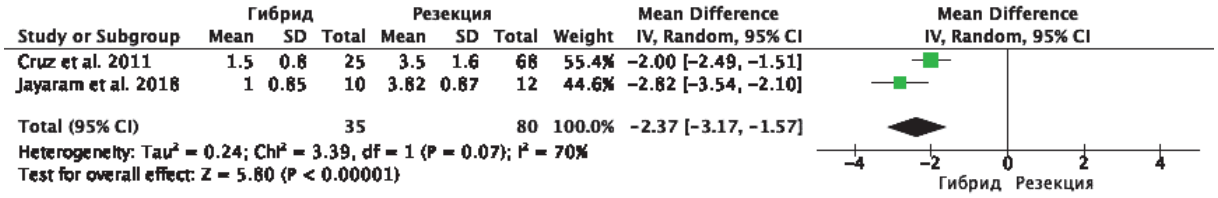

Figure 13. *Duration of the postoperative bed day in groups*

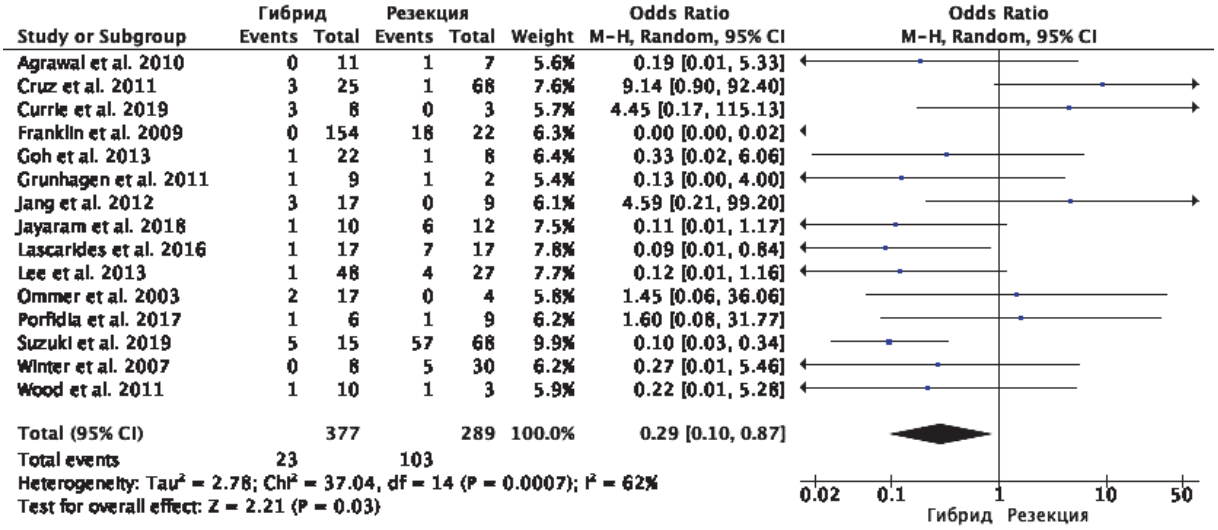

Figure 14. *The probability of detecting adenocarcinoma according to the pathomorphological study of the surgical preparation in groups*

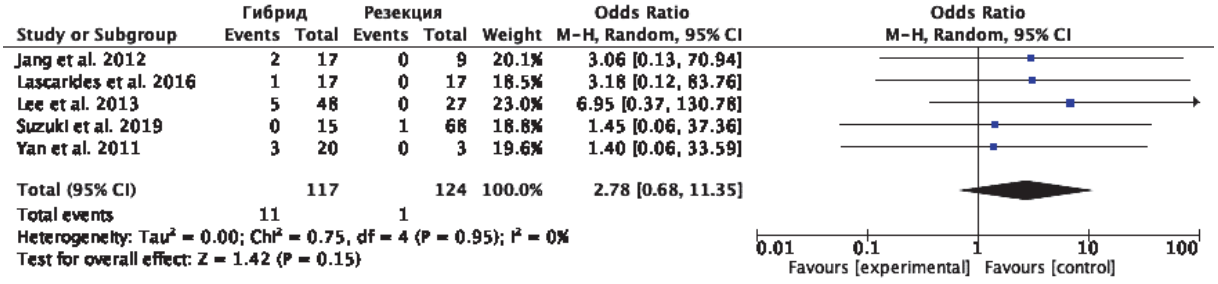

Figure 15. *The probability of local recurrence of neoplasm in groups*

DISCUSSION

The meta-analysis provides a comparative assessment of the effectiveness and safety of hybrid laparo-endoscopic operations and laparoscopic resections of the colon in the treatment of patients with benign neoplasms that cannot be removed endoscopically.

According to most publications available in the literature, the operation time and the hospital stay after hybrid laparo-endoscopic interventions turned out to be shorter in comparison with laparoscopic segmental resections of the colon [18–20,27,33], which is confirmed by results included in this meta-analysis [16,17,24,28].

We did not find significant differences in the likelihood of postoperative complications when using the compared treatment methods (OR = 0.7; 95% CI 0.38–1.53; $p = 0.44$). The incidence of complications did not differ between groups.

Previously, other authors made conclusions on comparable incidence of complications after the use of hybrid operations and laparoscopic resections of the colon [21,25,31].

As one of the most important safety parameters of the treatment methods used, this meta-analysis examined the reoperations rate for complications that have developed. In the main group it was 4%, and in the control group — 4.1%. The probability of performing reoperation for complications in both groups was not statistically significantly different (OR = 0.7; 95% CI 0.23–2.38; $p = 0.62$) [1,6,12,13,17,19,28,34].

Reoperations for oncological indications occurred in 19 (8.3%) of 227 patients who underwent hybrid operations [11,13,15,17,24,28,33,35], in whom, according to the results of pathomorphology of removed specimens, the tumor was represented by adenocarcinoma with a depth of invasion into the intestinal wall greater than T1sm1, and there was also lymphovascular and vascular invasion.

These data correlate with the publications by Arezzo (2015) and Placek (2017), in which the rate of detection of invasive cancer and the need for reoperations to achieve oncological radicality was 3.3 — 11% [2, 27].

It is worth emphasizing the possible limitations of our meta-analysis, which are due to the insufficient quality of the studies presented. This can be illustrated by the fact that the chance of detecting adenocarcinoma in the surgical specimen was 30% higher when performing standard laparoscopic segmental resection of the colon than in the group of hybrid operations [1,6,8,11–13,16,17,19,20,24,28,31,34,35]. A possible reason for such differences, given that the vast majority of available works on this topic are retrospective, may be a bias associated with the selection of patients with large tumors suspicious for malignancy for an obviously more radical segmental resection of the colon.

In 2015, Arezzo A. et al. published the results of a systematic literature review with meta-analysis, which included 11 single-center, non-randomized studies [2]. In this study, the rate of reoperations after hybrid laparo-endoscopic tumor removal to achieve oncological radicality was 7.9%. To eliminate surgical complications, reoperations occurred in 3.5% of cases. The presented data correlate with the results of this study: the rate of colon resection for oncological indications after hybrid operations was 8.3%, and reoperations for complications were performed in 4% of cases.

According to 5 studies included in the meta-analysis, in which the incidence of local recurrence was assessed, the rate was 9.4%, while all recurrent tumors were represented by adenomas [16,19,20,31,36], which correlates with results of most reports available in the literature.

It is impossible not to reflect the limitations of this meta-analysis due to the fact that the vast majority of studies included in it are retrospective, of unsatisfactory quality, with a high risk of bias studies. It included only 1 randomized trial with a small sample of patients. All this indicates the need for randomized studies to compare the results of hybrid laparo-endoscopic operations and laparoscopic resections of the colon for endoscopically unremovable tumors.

CONCLUSION

A meta-analysis of the effectiveness and safety of hybrid laparo-endoscopic operations in the treatment of patients with benign neoplasms of the colon demonstrated a comparablerate of postoperative complications, reoperations for complications, as well as mortality. However, in a number of patients there is the need to perform resection for oncological indications after hybrid operations. The use of hybrid procedures makes it possible to reduce the operation time and hospital stay.

AUTHORS CONTRIBUTION

Concept and design of the study: *Oleg I. Sushkov, Evgeniy S. Surovegin*.
Processing of the material: *Aleksey V. Kolosov*
Writing of the text and statistical data processing: *Aleksey V. Kolosov, Evgeniy S. Surovegin, Roman Yu. Khryukin*
Editing: *Oleg I. Sushkov, Sergey I. Achkasov*

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