



## Outcome after Right Hemicolectomy with Special Focus on Anastomotic Leakage – A Retrospective Analysis on 641 Patients

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### Abstract

**Introduction:** The right-sided hemicolectomy is a regularly performed abdominal surgery worldwide. Reasons for possible complications and the technique of the anastomosis, especially the occurrence of Anastomotic Leakage (AL), are still discussed controversially in the literature and considered a life threatening complication. Therefore, we analyzed our data retrospectively with special focus on anastomosis related complications.

**Material and Methods:** All patients who underwent a right hemicolectomy between 2010 and 2019 at the Department of General and Visceral Surgery at the Kepler University Clinic (KUK) – Med Campus III in Linz, Austria have been analyzed retrospectively. The following parameters were documented: Sex, age, BMI, indication for surgery, surgical approach, postoperative morbidity and mortality, technique of anastomosis, occurrence of AL, need for ileostomy, intraoperative peritonitis, postoperative revisional surgery, postoperative food intake, intraoperative peritonitis, corticosteroid intake at time of surgery, pain catheter, highest postoperative CRP level, lymph node stage (N) and the number of retrieved lymph nodes (in general and positive ones).

**Results:** Of 641 patients, 263 (41.0%) had laparoscopic resection (7.2% conversion rate) and 378 (59.0%) underwent open surgery. 239 (37.3%) of all patients got a hand-sewn anastomosis, whereas 375 (58.5%) received stapled ones which were mostly created extra-corporally. 26 (4.06%) patients got a terminal ileostomy and were therefore excluded from other calculations, resulting in a final patient collective of n=615. The overall leakage rate was 3.9% (n=24) with a postoperative mortality of 16.7% (4 of 24 patients with leakage, p=0.015\*). The occurrence of an AL was followed by average 1.92 (from 1 up to 8) revisional surgeries (p<0.001\*\*) between the 8<sup>th</sup> and 9<sup>th</sup> postoperative day. Eight (33.3%) of the leaking anastomosis were hand-sewn and 16 (66.7%) were stapled in acute (45.8%) or elective surgeries (54.2%).

**Conclusion:** The event of AL after right-sided hemicolectomy was rarely occurring and independent of the surgical approach as well as the anastomosis technique. Statistically significant differences in patients with leaks were found in the number of revisional surgeries, the ASA score, the postoperative 30-day morbidity and mortality, the length of the postoperative stay in hospital, highest postoperative CRP level and number of retrieved positive lymph nodes.

### Introduction

Colorectal cancer is one of the most common malignant diseases worldwide, accounting for more than 500,000 deaths annually [1]. It is the most common malignant tumor of the digestive tract, making up 8% to 10% of all cancer diagnosis. With a constantly increasing incidence, right sided malignancies occur in about 35% what makes the right hemicolectomy a regularly performed surgery world-wide [2,3].

Nevertheless, peri- or post-operative complications may occur. One of the most feared complications is AL that can be subsequently accompanied by an increased risk of postoperative morbidity, mortality, overall impact on the functional and oncological outcome and higher demands in hospital resources [4]. The etiology of AL is multifactorial and leakage rates regarding ileocolonic anastomosis are documented between 6.4% and 8.8% [1,5-7] and are therefore surprisingly high compared to the leakage rates of left hemicolectomy (AL rate of 1.9% to 6.5%) [1,7,8].

Since more than a century of investigation on risk factors for AL, some risk factors like male

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gender, obesity, a bigger tumor size or increased TNM staging and intraoperative complications have been firmly justified by several studies. Other risk factors like the anastomotic technique or surgical approach are to be discussed [4,9].

## Material and Methods

For this study, data of all patients who underwent right hemicolectomy between the years 2010 and 2019 at the Department of General and Visceral Surgery at the KUK – Med Campus III in Linz, Austria have been acquired retrospectively. Demographic data and information on sex, age, BMI, surgery indication, surgical approach, postoperative morbidity and mortality, anastomosis technique, occurrence of AL, need of ileostomy and postoperative revisional surgery, postoperative food intake, intraoperative peritonitis, corticosteroid intake at time of surgery, pain catheter, highest postoperative CRP, lymph node stage (N) and the number of retrieved lymph nodes (in general and positive ones) were statistically analyzed.

Postoperative morbidity was categorized using the Clavien-Dindo classification (grade 0 to 5) [10]. The lymph node stage was divided into classes using the TNM classification [11] and the ASA score [12] was used for the pre-operative health status.

In this study as well as in others [4], an AL is defined as a defect of the intestinal wall at the anastomotic site (including suture and staple lines) followed by communication between the intra- and extraluminal compartments.

The stapled anastomosis was mostly created extra-corporally, unisoperistaltic and side-to-side using the Medtronic Signia (Medtronic Österreich GmbH, Handelskai 94-96, 1200 Vienna, Austria) stapler with a violet cartridge (60 mm), whereas the hand-sewn ones were sutured isoperistaltic, in a single layer with a seromuscular running Monosyn suture.

### Statistical analysis

All data of continuous variables were checked for normal distribution (test of normality: Kolmogorov-Smirnov with Lilliefors significance correction, type I error =10%) variables with normally distributed data were compared by the t-test for independent samples. For variables without normally distributed data and for variables measured on ordinal scales the Mann-Whitney U test (exact or asymptomatic version) was used. Dichotomous variables were compared by the Fisher's exact test, the other categorical variables by the chi-square test (exact or with Monte Carlo simulation). Missing values were not replaced.

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The influence of the anastomosis technique, age, BMI, ASA score, sex, surgical indication, surgical approach, anastomotic technique, postoperative food intake, pain catheter, peritonitis, highest postoperative CRP level and number of retrieved lymph nodes (in general and positive ones) on AL was investigated by logistic

regression analyses (stepwise forward based on the likelihood ratio approach).

Since the type I error was not adjusted for multiple testing, the results of inferential statistics are only descriptive and the use of the term "significant" in the description of the study results always reflects only a local  $p < 0.05$  but no error probability below 5%. Statistical analysis was performed using the open-source R statistical software package, version 3.6.1 (The R Foundation for Statistical Computing, Vienna, Austria).

## Results

In total, 641 patients underwent right hemicolectomy. 263 (41.0%) had laparoscopy (with 7.2% conversion rate,  $n=19$ ) and 378 (59.0%) had open surgery. A number of 26 (4.06%) patients who got a terminal ileostomy were excluded from further calculations, ending up with a final patient collective of  $n=615$ . 239 patients received a hand-sewn (38.9%) and 375 a stapled anastomosis (61.1%) that was made extra-corporally in most cases (99.8%). Demographic and medical data is shown in Table 1.

42.7% of the patient collective had laparoscopy with a conversion rate of 6.9%, whereas 57.3% had open surgery done. 58.8% underwent elective surgery, in 41.2% there was an acute surgical indication (Table 2). 46.3% were female, 53.8% male patients (Table 1).

Most patients (89.3%) had pre-operative ASA score 2 or 3. Comparing patients with and without AL, patients in the leakage group had a significantly worse ASA score ( $p=0.044^*$ ) (Table 3).

The overall 30-day postoperative mortality was 4.2%. The leakage rate accounted for 3.9% with a significantly higher 30-day postoperative mortality of 16.7% ( $p=0.015^*$ ). 42.2% of all patients had no postoperative complications. The 30-day postoperative morbidity was 57.8%. 8.5% of all patients had revisional surgery (Table 3).

Referring to the technique of anastomosis (Table 2), 38.9% of patients received hand-sewn anastomosis, whereas 61.1% of the anastomosis were stapled. Most of them were placed side-to-side (87.0%), some end-to-side (10.7%) and only a small number was created end-to-end (2.3%).

325 patients had surgery due to malignancy. 56.8% of them had a N0 resection, 15.4% N1 resection and 27.7% ended up with a N2-N4 resection. In average, 20.39 lymph nodes were removed in general, 1.92 were tumor positive lymph nodes (Table 1).

In an univariate subgroup analysis between the leakage and non-leakage group, similar results were found concerning the following parameters: Anastomosis technique (hand-sewn vs. stapled and side-side vs. end-side vs. end-end), age, BMI, sex, indication for surgery, surgical approach, protective ileostomy, postoperative day of first surgical revision, postoperative start with a light to normal diet, retrieved lymph nodes in general, the lymph node stage (TNM), corticosteroids intake, peritonitis and pain catheter. However, there were statistically significant differences in the leakage group regarding the number of revisional surgeries, the ASA score, the postoperative 30-day morbidity and mortality, the length of the postoperative stay in hospital, highest postoperative CRP and number of retrieved positive lymph nodes (Table 4).

In a multivariate regression analysis approach, postoperative CRP is the only covariate with a clear influence on anastomotic leakage ( $p=0.007$ ; Odds Ratio =1.111 (two-sided 95% confidence interval

**Table 1:** Demographic and medical data of final patient collective (missing values were not replaced).

| Parameter  |              | Female         |   | Male                                      |                |                           |             |
|--|--------------|----------------|---|---|----------------|---------------------------|-------------|
| <b>Sex</b>   | All patients | 284 (46.3%)    |   | 331 (53.8%)                               |                |                           |             |
|  | No leakage   | 275 (46.5%)    |   | 316 (53.5)                                |                |                           |             |
|  | Leakage      | 9 (37.5%)      |   | 15 (62.5%)                                |                |                           |             |
|  |              | <b>Minimum</b> | <b>Median</b>                                       | <b>Average</b>                            | <b>Maximum</b> | <b>Standard deviation</b> |             |
| <b>Age</b>   | All patients | 20.00          | 71.00   | 68.32                                     | 93.00          | 13.57                     |             |
|  | No leakage   | 20.00          | 71.00   | 68.26                                     | 93.00          | 13.69                     |             |
|  | Leakage      | 46.00          | 69.00   | 69.96                                     | 89.00          | 10.26                     |             |
| <b>BMI</b>   | All patients | 14.00          | 26.00   | 26.20                                     | 47.00          | 4.71                      |             |
|  | No leakage   | 14.00          | 26.00   | 26.15                                     | 47.00          | 4.65                      |             |
|  | Leakage      | 17.80          | 27.10   | 27.33                                     | 39.00          | 5.89                      |             |
| <b>Postoperative stay at hospital in days</b>  | All patients | 1.00           | 10.00   | 13.74                                     | 99.00          | 10.69                     |             |
|  | No leakage   | 1.00           | 10.00   | 13.01                                     | 77.00          | 9.19                      |             |
|  | Leakage      | 18.00          | 24.00   | 35.42                                     | 99.00          | 23.32                     |             |
| <b>Number of revisional surgeries</b>  | All patients | 0.00           | 0.00  | 0.17                                      | 8.00           | 0.60                      |             |
|  | No leakage   | 0.00           | 0.00  | 0.10                                      | 3.00           | 0.39                      |             |
|  | Leakage      | 1.00           | 1.00  | 1.92                                      | 8.00           | 1.59                      |             |
| <b>Postoperative day of first revisional surgery</b>                                 | All patients | 0.00           | 6.50  | 7.92                                      | 38.00          | 7.14                      |             |
|  | No leakage   | 0.00           | 5.50  | 7.43                                      | 33.00          | 6.93                      |             |
|  | Leakage      | 2.00           | 7.00  | 8.79                                      | 38.00          | 7.58                      |             |
| <b>Postoperative start with a light to normal diet in days (paralysis parameter)</b> | All patients | 2.00           | 4.00  | 4.59                                      | 33.00          | 2.82                      |             |
|  | No leakage   | 2.00           | 3.00  | 4.57                                      | 12.00          | 2.81                      |             |
|  | Leakage      | 2.00           | 4.00  | 5.18                                      | 33.00          | 3.03                      |             |
| <b>Highest postoperative CRP</b>   | All patients | 0.50           | 15.30   | 17.36                                     | 87.00          | 10.66                     |             |
|  | No leakage   | 0.50           | 15.00   | 16.88                                     | 87.00          | 10.40                     |             |
|  | Leakage      | 3.20           | 28.45   | 29.10                                     | 51.10          | 10.46                     |             |
| <b>Number of retrieved positive lymphatic nodes</b>                                  | All patients | 0.00           | 0.00  | 1.92                                      | 23.00          | 3.78                      |             |
|  | No leakage   | 0.00           | 0.00  | 1.87                                      | 13.00          | 3.74                      |             |
|  | Leakage      | 0.00           | 2.00  | 4.13                                      | 23.00          | 5.00                      |             |
| <b>Number of retrieved lymphatic nodes in general</b>                                | All patients | 0.00           | 18.00   | 20.39                                     | 74.00          | 9.83                      |             |
|  | No leakage   | 4.00           | 18.00   | 20.32                                     | 57.00          | 9.71                      |             |
|  | Leakage      | 0.00           | 21.00   | 22.82                                     | 74.00          | 14.03                     |             |
|  |              | <b>N0</b>      | <b>N1</b>   | <b>N2</b>                                 | <b>N3</b>      | <b>N4</b>                 |             |
| <b>Lymphatic nodal stage in malignancies (TNM classification)</b>                    | All patients | 185 (56.8%)    | 50 (15.4%)  | 87 (26.8%)                                | 1 (0.3%)       | 2 (0.6%)                  |             |
|  | No leakage   | 184 (57.7%)    | 47 (94.0%)  | 85 (97.7%)                                | 1 (0.3%)       | 2 (0.6%)                  |             |
|  | Leakage      | 1 (16.7%)      | 3 (6.0%)  | 2 (2.3%)                                  | 0 (0.0%)       | 0 (0.0%)                  |             |
|  |              | <b>Yes</b>     | <b>No</b>   | Peritonitis                               | <b>Yes</b>     | <b>No</b>                 |             |
| <b>Long-term corticosteroid intake at time of surgery</b>                            | All patients | 36 (6.1 %)     | 557 (93.9%)   |   | All patients   | 67 (10.9%)                | 546 (89.1%) |
|  | No leakage   | 33 (5.8%)      | 527 (94.2%)   |   | No leakage     | 64 (10.9%)                | 525 (89.1%) |
|  | Leakage      | 3 (13.0%)      | 20 (87.0%)  | Leakage                                   | 3 (12.5%)      | 21 (87.5%)                |             |
|  |              | <b>None</b>    | <b>Patient-Controlled Epidural Analgesia (PCEA)</b> | <b>Patient-Controlled Analgesia (PCA)</b> |                |                           |             |
| <b>Pain catheter</b>   | All patients | 254 (43.5%)    | 232 (39.7%)   | 98 (16.8%)                                |                |                           |             |
|  | No leakage   | 243 (43.2%)    | 227 (40.4%)   | 92 (16.4%)                                |                |                           |             |
|  | Leakage      | 11 (50%)       | 5 (22.7%)   | 6 (27.3%)                                 |                |                           |             |

**Table 2:** Indication for surgery. Surgical approach and technique of anastomosis.

| Parameter                |                  | Laparoscopy [conversion] |               | Open surgery         |              |             |             |
|--------------------------|------------------|--------------------------|---------------|----------------------|--------------|-------------|-------------|
| Surgical approach        | All patients     | 262 (42.7%) [18 (6.9%)]  |               | 352 (57.3%)          |              |             |             |
|                          | No leakage       | 252 (42.6%) [16 (6.3%)]  |               | 339 (54.4%)          |              |             |             |
|                          | Leakage          | 10 (41.7%) [2 (2.0%)]    |               | 14 (58.3%)           |              |             |             |
| Indication for surgery   | Elective surgery |                          | Acute surgery |                      |              |             |             |
|                          | All patients     | 362 (58.9%)              |               | 253 (41.1%)          |              |             |             |
|                          | No leakage       | 349 (59.1%)              |               | 242 (40.9%)          |              |             |             |
|                          | Leakage          | 13 (54.2%)               |               | 11 (45.8%)           |              |             |             |
| Technique of anastomosis |                  | Hand-sewn                | Stapled       | Side-side            | End-side     | End-end     |             |
|                          | All patients     | 239 (38.9%)              | 375 (61.1%)   | 527 (87.0%)          | 65 (10.7%)   | 14 (2.3%)   |             |
|                          | No leakage       | 231 (39.2%)              | 359 (60.8%)   | 505 (86.8%)          | 63 (10.8%)   | 14 (2.3%)   |             |
|                          | Leakage          | 8 (33.3%)                | 16 (66.7%)    | 22 (91.7%)           | 2 (8.3%)     | 0 (0.0%)    |             |
| Anastomotic leakage      |                  | No leakage               | Leakage       | Protective ileostomy | Ileostomy    | None        |             |
|                          | All patients     | 590 (96.1%)              | 24 (3.9%)     |                      | All patients | 3 (0.5%)    | 611 (99.5%) |
|                          | No leakage       |                          |               |                      | No leakage   | 3 (0.5%)    | 587 (99.5%) |
|                          | Leakage          |                          |               | Leakage              | 0 (0.0%)     | 24 (100.0%) |             |

**Table 3:** Preoperative ASA score. Postoperative 30-day morbidity and mortality.

| Parameter                                      |              | ASA 1          | ASA 2       | ASA 3       |           | ASA 4         |           | ASA 5    |           |
|--|--------------|----------------|-------------|-------------|-----------|---------------|-----------|----------|-----------|
| ASA score                                      | All patients | 26 (5.0%)      | 244 (47.4%) | 216 (41.9%) |           | 28 (5.4%)     |           | 1 (0.2%) |           |
|  | No leakage   | 26 (5.2%)      | 239 (48.1%) | 204 (41.0%) |           | 27 (5.4%)     |           | 1 (0.2%) |           |
|  | Leakage      | 0 (0.0%)       | 5 (27.8%)   | 12 (66.7)   |           | 1 (5.6%)      |           | 0 (0.0%) |           |
| 30-day postoperative morbidity (Clavien-Dindo) |              | 0              | 1           | 2           | 3a        | 3b            | 4a        | 4b       | 5         |
|  | All patients | 259 (42.1%)    | 67 (10.9%)  | 167 (27.2%) | 30 (4.9%) | 52 (8.5%)     | 12 (2.0%) | 2 (0.3%) | 26 (4.2%) |
|  | No leakage   | 258 (43.7%)    | 67 (11.3%)  | 167 (28.3%) | 30 (5.1%) | 37 (6.3%)     | 8 (1.4%)  | 2 (0.3%) | 22 (3.7%) |
|  | Leakage      | 1 (4.2%)       | 0 (0.0%)    | 0 (0.0%)    |           | 15 (62.5%)    | 4 (16.7%) | 0 (0.0%) | 4 (16.7%) |
| 30-day postoperative mortality                 |              | Mortality rate |             |             |           | Survival rate |           |          |           |
|  | All patients | 26 (4.2%)      |             |             |           | 589 (95.8%)   |           |          |           |
|  | No leakage   | 22 (3.7%)      |             |             |           | 569 (96.3%)   |           |          |           |
|  | Leakage      | 4 (16.7%)      |             |             |           | 20 (83.3%)    |           |          |           |

=1.026-1.200)).

## Discussion

Interpreting our study results, the event of an AL after right hemicolectomy was rarely occurring with a leakage rate of 3.9% and independent of the surgical approach as well as the anastomosis technique. Several studies [1,13] found hand-sewn and stapled anastomosis to be equally safe. In contrast, Frasson et al. [9] presented a higher risk of AL for stapled ones. A large multicenter study [14] and a meta-analysis [15], however, found a higher leak rate in patients with hand-sewn ileocolonic anastomosis. The type of the anastomosis is still a controversially discussed topic and no clear recommendation for the surgical procedure can be given.

Although, corticosteroids intake is known to be a risk factor for AL after left-sided hemicolectomies and rectal resections [16,17], we could not prove a higher risk for AL in our patients with long-term corticosteroids intake after right-sided hemicolectomy. In our study, we defined a corticosteroids intake not only as an oral or intravenous intake, but also as an inhalative intake, what might have affected our

statistical results.

In our study, the number of retrieved positive lymph nodes was a significant factor regarding the occurrence of AL, whereas the lymph node stage and the number of retrieved lymph nodes in general were not. It is known that the number of retrieved lymph nodes in general is associated with a higher tumor stage and tumor size but there is no known association between the retrieved positive lymph nodes and the incidence of AL [18]. Several studies [19-21] comparing conventional colectomy with complete mesocolic excision/extended lymphadenectomy for colon cancer could not find statistically significant differences in leakage rates, the 30-day postoperative morbidity and mortality or occurrence of postoperative complications.

In contribution, we did not document how experienced the surgeon was and if there was an influence on the surgery outcome. However, a resident never performed an anastomosis without the guidance of an experienced senior surgeon. According to Marinello et al. [22] the individual surgeon and his or her experience matters regarding AL.

**Table 4:** Univariate subgroup analysis (\*...p<0.05; \*\*... p<0.01).

| Parameter   | P-value            |
|---|--------------------|
| Age   | 0.873              |
| ASA score   | <b>0.044*</b>      |
| BMI   | 0.326              |
| Corticosteroids intake  | 0.158              |
| Hand-sewn vs. stapled anastomosis   | 0.672              |
| Highest postoperative CRP   | <b>&lt;0.001**</b> |
| Indication for surgery  | 0.675              |
| Number of retrieved positive lymph nodes                                      | <b>0.018*</b>      |
| Number of retrieved lymph nodes in general                                    | 0.639              |
| Number of revisional surgeries  | <b>&lt;0.001**</b> |
| Pain catheter   | 0.187              |
| Peritonitis   | 0.738              |
| Postoperative 30-day morbidity (Clavien-Dindo)                                | <b>&lt;0.001**</b> |
| Postoperative 30-day mortality  | <b>0.015*</b>      |
| Postoperative day of first revisional surgery                                 | 0.240              |
| Postoperative start with a light to normal diet in days (paralysis parameter) | 0.592              |
| Postoperative stay in hospital in days  | <b>&lt;0.001**</b> |
| Protective Ileostomy  | >0.999             |
| Sex   | 0.412              |
| Side-side vs. end-side vs. end-end anastomosis                                | 0.698              |
| Surgical approach   | 0.227              |
| TNM classification of retrieved positive lymph nodes                          | 0.069              |

## Conclusion

In conclusion, right hemicolectomy is a safe procedure with a low morbidity and mortality regardless the operative technique. The type of anastomosis did not influence the leakage rate. The ASA score of the patient and the number of retrieved lymph nodes are the most factors influencing the overall outcome.

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