

Surgery for colorectal cancer in elderly patients: is there such a thing as being too old?

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SUMMARY: Surgery for colorectal cancer in elderly patients: is there such a thing as being too old?

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Introduction. *The overall increase in life expectancy causes a rapid increase in number of elderly patients needing colorectal surgery. It remains unclear if there is a significant risk factor in patients over 80 years of age for postoperative morbidity and mortality. For this reason we investigated the perioperative, outcome and long-term survival after surgery for colorectal cancer in our hospital.*

Materials and methods. *We retrospectively analysed a database containing information about patients who underwent surgery for colorectal cancer from January 2010 to December 2015 at the St. Bernhard Hospital in Kamp-Lintfort, Germany. The last follow-up date was 31th of December 2017.*

Results. *A total of 232 patients were enrolled and analysed in this study. All patients were separated in two groups depending in age. The first group was ≥ 80 years old ($n=49$). The second group was < 80 years old ($n=183$). High ASA-Scores (≥ 3) were detectable more often in elderly patients ($p<0,05$). Elderly and young patients had a similar risk for postoperative anastomotic leakages ($p=0,047$). Likewise there were no significant differences regarding the Dindo-Clavien-Classification ($p=0,13$). The mortality within the first 30 days after surgery was significant elevated for elderly patients compared to younger patients ($p=0,04$). Also the overall 1-year survival was 90% for the younger and 73,5% for the older study group ($p<0,05$).*

Conclusion. *Both the short-term outcome and long-term survival rate after colorectal surgery for cancer are worse for patients older than 80 years of age. After interpretation of all data it remains unclear if the age itself is still the biggest risk factor. When old patients have a good ASA-Score and no severe comorbidities, colorectal surgery remains safe even for patients older than 80 years.*

KEY WORDS: Elderly patients - Colorectal surgery - Colorectal cancer.

Introduction

The overall increase in life expectancy, especially in countries with highly developed health care, causes a rapid increase in number of elderly patients needing colorectal surgery (1). Colorectal cancer is still the third most frequent cancer-related cause of death and complete resection in patients regardless what age remains essential for the potential cure of this cancer (2).

The total number of elderly patients is growing worldwide. Within this study patients ≥ 80 years of age represent the fastest growing subpart. But even the management of colorectal surgical issues becomes more challenging for these patients (3).

Despite this fact, previous studies have often excluded patients older than 80 years. Especially publications older than 10 years defined older patients undergoing surgery often as patients older than 60 years (3-5). But nowadays our main concern in everyday practice relates to the patients with age ≥ 80 years. This advanced age is considered an important and independent risk-factor for postoperative morbidity and mortality (5-7). The perioperative high-risk constellation caused by significant comorbidity results in a poor postoperative outcome. The coincidence of pulmonary and cardiovascular diseases is

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significantly increased in elderly patients and determines the main causes of postoperative morbidity.

At the same time, however, no differences in intraoperative complications for older patients have been published (8). Surgery in elderly patients is not necessarily associated with a higher rate of surgical related complications and still remains safe (9, 10).

Although a couple of studies were designed to evaluate the safety of colorectal surgery of elderly patients, the problem of the term elderly being very subjective remains and is influenced by the country, the health-care system and personal experience of every surgeon. A European survey from 2016 conducted amongst geriatric educated surgeons has shown that almost all surgeons offer surgery regardless of the patient's age. However, even in this experienced group of surgeons the definition of older aged patients remains controversial. 30% of respondents defined patients older than 70 years as old, 32% patients ≥ 75 years and 25% of these surgeons patients older than 80 years (11).

Over the last years our impression was, that there is a significant risk factor in patients over 80 years of age for postoperative morbidity and mortality. For this reason we retrospectively investigated the perioperative, outcome and long-term survival after surgery for colorectal cancer in patients ≥ 80 years and compared them with patients younger than 80 years. Neither oldest patients nor patients with pre-existing multiple comorbidities were excluded.

Materials and methods

All patients who had undergone surgery for colorectal cancer between 2010 and 2015 at the Department of Surgery, St. Bernhard Hospital, Kamp-Lintfort, Germany were prospectively collected in a database. The last date of inclusion was December 2015. The last date of follow-up was 31.12.2017. The Institutional Review Board Approval for collecting the prospective data and retrospective review of the patient charts for this project were obtained from the competent Ethical Committee. Patients were divided into 2 Groups according to age. Group A were aged ≥ 80 years and patients in Group B were aged < 80 years. The data set for each patient included age, sex, ASA-Score, duration of surgery, length of pre- and postoperative hospital stay, tumor staging, postoperative complications (Dindo-Clavien classification, anastomotic leakage, wound infection), 30-day mortality, follow-up mortality.

Statistical analysis

Statistical testing was performed using IBM® SPSS® statics Version 19 (SPSS Inc., IBM Corporation Software Group, Somers, NY, USA). The distribution of nominal or ordinal scaled variables was compared by Q-Q-Plots. Cardinal variables were tested for normal distribution by visualization on a histogram and by the Kolmogorov–Smirnov test. For comparison of independent groups, the t test was used for normal distribution additionally the Fischer exact test and the Chi-Square test. All tests were performed two-sided, and p values less than 0.05 were considered to be statistically significant. No correction of p values was applied to adjust for multiple test issues. Time-dependent survival probabilities were estimated with the Kaplan–Meier method and the log-rank test was used to compare subgroups. To investigate the effect on survival of multivariable relationships among covariates, Cox proportional hazard models were used. Survival times as well as estimated hazard ratios (HRs) were calculated and reported in 95 % confidence intervals (CIs). Performed statistical tests are indicated if not self-explanatory.

Results

Patient data

Between 2010 and 2015, 232 patients underwent surgery for colorectal cancer at our institution. Inclusion criteria were a histologically proven colorectal cancer and surgical resection of the including lymph node dissection. Only patients undergoing single procedure receiving palliative care stoma were excluded. Of all patients there were 131 (56.5%) men and 101 women (43.5%). The median age was 72 years (youngest patient 38 years, oldest patient 93 years) (Table 1). All patients were separated in two groups depending on age. The first group was ≥ 80 years old (n=49). The second group was < 80 years old (n= 183). High ASA-Scores were detectable more often in elderly patients (ASA III 82% vs. 60%; ASA IV 8% vs. 1.6%, $p < 0,05$). The patient characteristics are summarized in Table 2.

Staging and histopathological findings

The UICC tumor stage was stage I in 17 % (n = 40), stage II in 38 % (n = 88), stage III in 30 % (n = 69), and stage IV in 15 % (n = 35). There were no detectable differences between both group of pa-

TABLE 1 - AGE DISTRIBUTION OF THE INVESTIGATION.

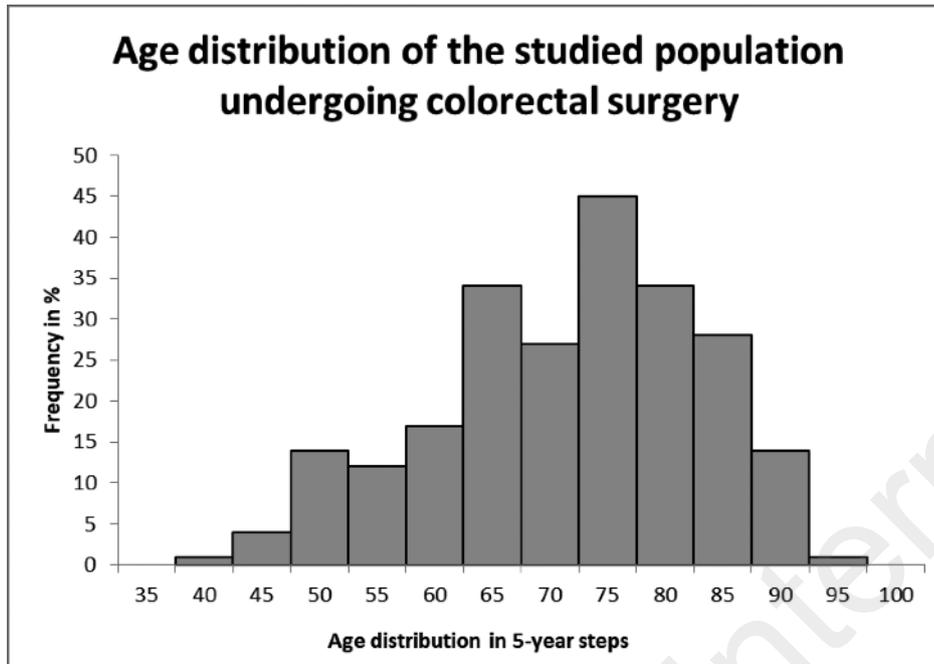


TABLE 2 - CHARACTERISTICS OF INVESTIGATED PATIENTS [MEDIAN RANGE OF AGE, NUMBER OF PATIENTS IN EACH GROUP (PERCENTAGE)].

| Characteristics | Group A (≥ 80 years) (n=49) | Group B <80 (years (n=183) | P-value |
|-----------------|-----------------------------|----------------------------|---------|
| Age (years) | | | |
| Median | 83 | 67 | - |
| (range) | (80 – 93) | (38 – 79) | |
| Sex | | | 0.26 |
| Male | 24 (49%) | 107 (58.5%) | |
| Female | 25 (51%) | 76 (41.5%) | |
| ASA-PS | | | <0,05 |
| 1 | 0 (0%) | 5 (2,8%) | |
| 2 | 5 (10,2%) | 60 (33,7%) | |
| 3 | 40 (81,6%) | 110 (61,8%) | |
| 4 | 4 (8,2%) | 3 (1,7%) | |

tients regarding the distribution of the tumor stage and tumor location (Table 3).

Perioperative data

The median length of preoperative hospital stay was 2 days. The preoperative hospital stay was longer for elderly patients (mean 8 ± 9 vs. 5 ± 6 days, p<0.05). Whereas the duration of the postoperative hospital stay was equal in both groups. Elderly patients of group A had more urgent operation procedures than group B (10.2% vs. 2.7%, p<0.05). Like-

wise the duration of the operative procedure was shorter for elderly patients (140 vs. 173, p<0.05) (Table 4).

Postoperative complications

Young and elderly Patients had a similar risk for anastomotic leakages (2% vs. 5.5% p= 0.47). Likewise there were no significant differences regarding the Dindo-Clavien classification for postoperative complications and the need for blood-transfusion during the stay in both groups (p= 0, 13) (Table 5).

TABLE 3 - TUMOR LOCATION AND HISTOPATHOLOGICAL FINDINGS.

| Characteristics | Group A (≥ 80 years) (n=49) | Group B <80 (years) (n=183) | P-value |
|--|-----------------------------------|-----------------------------|---------|
| Tumor location | | | 0.43 |
| Right-side colon | 20 (40.8%) | 62 (33.9%) | |
| Left-side colon | 21 (42.9%) | 80 (43.7%) | |
| Rectum (distal extension to 12cm from anal margin) | 8 (16.3%) | 41 (22.4%) | |
| T factor | | | 0.37 |
| T0 | 0 (0%) | 6 (3.3%) | |
| T1 | 4 (8.2%) | 13 (7.1%) | |
| T2 | 7 (14.3%) | 41 (22.4%) | |
| T3 | 29 (59.2%) | 103 (56.3%) | |
| T4a | 3 (6.1%) | 11 (6.0%) | |
| T4b | 6 (12.2%) | 9 (4.9%) | |
| N factor | | | 0.43 |
| Negative | 30 (61.2%) | 117 (63.9%) | |
| Positive | 19 (38.8%) | 66 (36.1%) | |
| UICC-Stage | | | 0.93 |
| 1 | 9 (18.4%) | 31 (16.9%) | |
| 2 | 20 (40.8%) | 68 (37.2%) | |
| 3 | 13 (26.5%) | 56 (30.6%) | |
| 4 | 7 (14.3%) | 28 (15.3%) | |

TABLE 4 - PERIOPERATIVE FINDINGS.

| Characteristics | Group A (≥ 80 years) | Group B <80 (years) | P-value |
|------------------------------------|----------------------------|---------------------|---------|
| Operation time median length (min) | 140 | 173 | <0.05 |
| Urgent surgery | | | <0,05 |
| Yes | 5 (10.2%) | 5 (2.7%) | |
| No | 44 (89.8%) | 178 (97.3%) | |

Survival analysis

The mortality within the first 30 days after surgery was significantly elevated for elderly patients compared to younger patients (10% vs. 2.7%, $p = 0.04$).

The overall 1-year survival was 90% for the younger and 73.5% for the older study group ($p < 0.05$) (Table 6).

The tumor-specific 5-year survival rate for all stages was 79.2% in the younger and 65.3% in the elderly patients ($p < 0.05$) (Table 7).

Discussion

The short- and long-term outcome of colorectal surgery in patients older than 80 years of age was significantly worse than the results of younger patients. Our results further validate our impression of previous years that there could be a significant risk factor in colorectal surgery for patients aged 80 years and older.

Previous studies have investigated the outcome of elderly patients and have described different re-

TABLE 5 - POSTOPERATIVE COMPLICATIONS.

| Characteristics | Group A (≥ 80 years) (n=49) | Group B <80 (years) (n=183) | P-value |
|-----------------------------------|-----------------------------------|-----------------------------|---------|
| Clavien-Dindo classification | | | 0.13 |
| 1 | 13 (26.5%) | 75 (41.0%) | |
| 2 | 17 (34.7%) | 70 (38.3%) | |
| 3a | 3 (6.1%) | 4 (2.2%) | |
| 3b | 5 (10.2%) | 14 (7.7%) | |
| 4a | 5 (10.2%) | 11 (6.0%) | |
| 4b | 2 (4.1%) | 5 (2.6%) | |
| 5 | 4 (8.2%) | 4 (2.2%) | |
| Blood-transfusion during stayover | | | 0.08 |
| Yes | 30 (61.2%) | 85 (46.4%) | |
| No | 19 (38.8%) | 98 (53.6%) | |
| Anastomic-leakage | | | 0.47 |
| Yes | 1 (2.0%) | 10 (5.5%) | |
| No | 48 (98.0%) | 173 (94.5%) | |

TABLE 6 - SURVIVAL PLOT 1 YEAR IN DAYS. SURVIVAL FOR GROUP A (>80 YEARS) AND GROUP B (<80 YEARS) DUE TO KAPLAN-MEIER ESTIMATION.

First year survival of the studied population undergoing colorectal surgery, separated by age

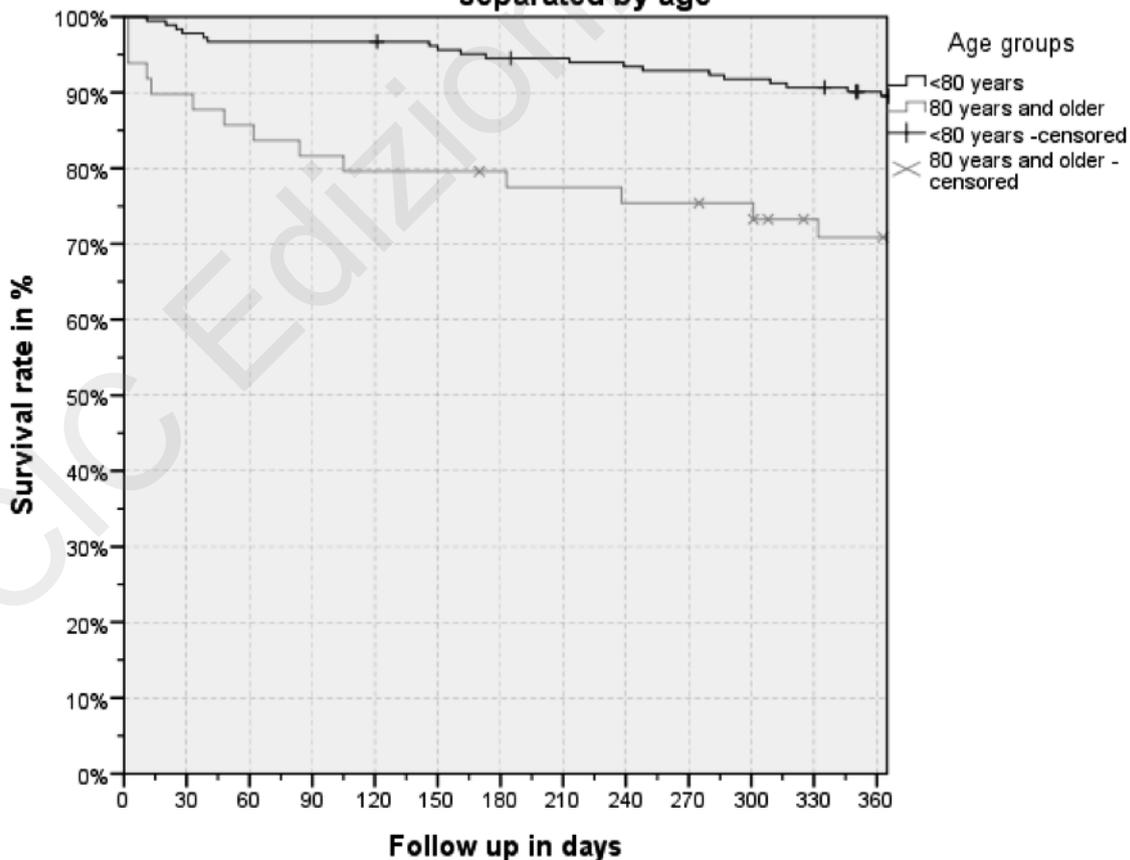
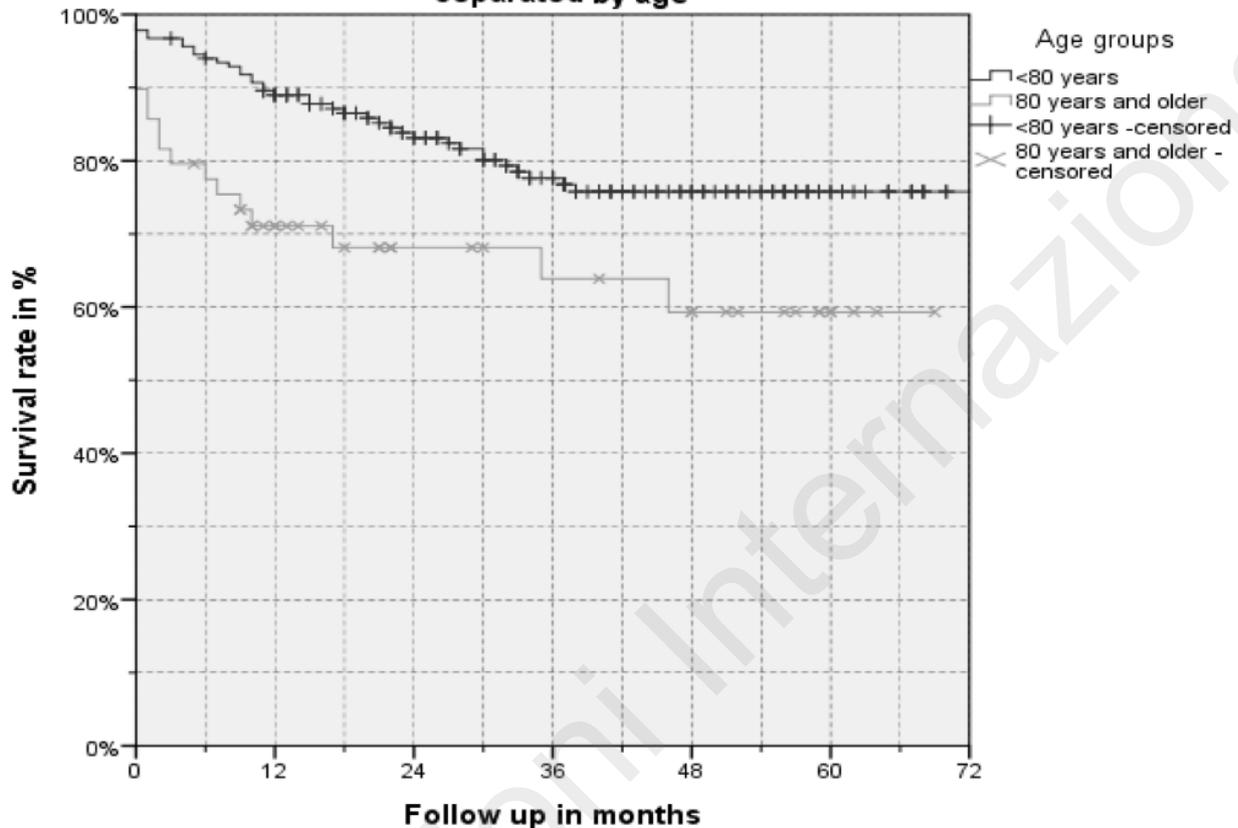


TABLE 7 - SURVIVAL PLOT 5 YEARS IN MONTHS.

Five years survival of the studied population undergoing colorectal surgery, separated by age



sults. Yukawa et al. reviewed their records of patients undergoing colectomy between March 2000 and April 2015. A total of 191 patients were investigated and divided into the two groups of elderly patients (Group A: 70 – 79 years) and extremely elderly patients (Group B: ≥ 80 years). 137 patients were classified elderly and 54 of them as extremely elderly. The 5-year overall survival rates were similar (75,6% vs. 76,9%, $p=0,554$). Postoperative complication rates in Group A and B were 12,4 and 16,7%, respectively and did not differ to a statistically significant extent ($p=0,44$) (3). Bircan et al. published a study which was conducted between January 2008 and December 2013. Among their patients undergoing colorectal surgery, 110 were between 60 and 69 years of age, 99 were between 70 and 79 years of age and 56 were older than 79 years. There were no significant differences in the postoperative surgical complications of the three groups (10,0, 13,1 and 21,4%, respectively) (10). Only the hospital stay for the extremely older patients was described as significantly longer ($p=0,009$).

Pelloni et al. evaluated their own records of colorectal procedures starting in 2002 and ending in 2008 (12). They divided their patients in groups of patients younger than 80 years and older than 80 years of age. The complications, mortality and length of hospital stay were similar.

A study conducted by Kang et al. reviewed age factor in postoperative outcome after laparoscopic resection of colorectal cancers in 578 patients (13). The patients were divided into 6 groups according to their age using 70, 75 and 80 years as cut-off values. The postoperative complication rates in the older groups were higher in all three age cut-off values. However, only the cut-off value of 80 years showed a significantly difference between the two groups. In addition, a trend towards more severe complications following the Dindo-Clavien classification was described for the oldest group with ages older than 80 years.

Especially in the last years the knowledge regarding less-invasive surgical procedures and the perioperative management in older patients has grown fast.

With the help of complex analysis current literature reveals that age alone does not influence surgery outcome, but rather that the higher number of comorbidities and compromised physical capacities to recover from perioperative complications play a greater role (14). Our study is consistent with the previously reviewed ones. Patients above 80 years old had severe comorbidities significantly more often, which resulted in a significantly higher percentage of ASA-Scores Level III and IV (ASA III 82% vs. 60%, ASA IV 8% vs. 1.6%, both $p < 0,05$). Statistical reasons don't allow individual assessment of the correlated age and ASA-Score, in regards to poorer outcome in our analysis. A multivariate ROC-analysis, for example, to isolate the factor age requires a much greater number than our study population. We will continue our prospective data collection and think about including other hospitals of our clinical network to achieve the minimum number for more complex analysis. Other factors such as staging and histopathological findings were shown to have no significant effect on the various outcomes. Especially the risk factors tumor location in the rectum and UICC-Stadium IV were divided evenly between both groups.

In our perioperative findings there was a significantly higher preoperative hospital stay for the older group. Patients aged over 80 years stayed in median 8 days before surgery. In our study, this was caused by more examinations through colleagues of other medical specialities being necessary, particularly cardiologists and pulmonologists. The duration of postoperative stays remained similar. This is consistent with previous reports from other working groups. Senagore et al. evaluated, that there was no difference between Patients older than 70 years compared with patients younger than 60 years of age (15).

Older patients with a left sided tumor location received an anastomosis less frequently than the younger patients. This resulted in the shorter medi-

an operation time for Group A (140 min vs. 173 min, $p < 0,05$). Another important perioperative finding was that acute revision was statistically necessary more often in the older Group A (10.2% vs 2.7%, $p < 0,05$). Patients presented themselves more often with an Ileus or a secondary perforation. This seems to be another good reason for poorer outcome. With a higher number of patients in our future study groups we expect to be able to represent this factor in an announced multivariate analysis.

Like Kang et al. described before, we detected a trend toward higher grades of complications following the Dindo-Clavien classification. However, no significant differences were seen for any stage of classification. The most obvious trend displays the number of needed blood-transfusions. Although there was no significant level shown, the trend could be caused by a less restrictive use of blood transfusion in our clinic for elderly patients.

The interpretation of our results needs special attention. Our present report was a prospectively conducted, but retrospectively analysed study. The study was only performed in a single center and not randomized. Furthermore the total number of patients enrolled in this study were not sufficient to enable us to perform a multivariate analysis.

Conclusion

In summary, both the short-term outcome and long-term survival rate after colorectal surgery for colorectal cancer are worse for patients older than 80 years of age. After interpretation of all collected data it remains unclear if the age itself is still the biggest risk factor. When they have a good ASA-Score and no severe comorbidities, colorectal surgery remains safe even for patients older than 80 years.

At all tumor resection and surgery seems justified also for patients older than 80 years.

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