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# Influence of Body Mass Index on Operability, Morbidity and Disease Outcome following Radical Cystectomy

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**Key Words**
Bladder cancer, complications · Bladder cancer patients, survival · Body mass index · Cystectomy · Radical cystectomy

**Abstract**
***Introduction:*** Obesity may influence postoperative outcome after tumor surgery. We evaluated the impact of patients' body mass index (BMI) on peri- and postoperative morbidity and outcome following radical cystectomy for bladder cancer. ***Patients and Methods:*** 390 consecutive patients who underwent radical cystectomy due to bladder cancer from January 1986 to December 2004 were reviewed. According to WHO criteria, patients were divided into normal weight (NW, 45.6%), overweight (OW, 44.4%) and obese (10.0%) subgroups. The BMI of patients was associated to the time of surgery, amount of intraoperative blood units, TNM stage, postoperative complication rate as well as overall survival. ***Results:*** The time of cystectomy increased with the degree of patients' obesity (NW, 330 min; OW, 355 min; p = 0.007). Between NW and OW patients no significant differences were noted in respect to intraoperative blood transfusion rate (NW, 3.0; OW, 2.0; p = 0.47), postoperative TNM stage (pTis–pT2b: 42.6 vs. 48.6%; pT3a–4: 38.2 vs. 27.2%; pN+: 20.2 vs. 24.2%) and postoperative complications, except for postoperative bleeding, which was more common in OW patients (p = 0.02). Mean overall survival times showed no significant differences between NW and OW patients receiving ileal conduits (5-year survival rate: 34.0 vs. 41.1%; p = 0.140) or ileal neobladders (5-year survival rate: 65.1 vs. 70.8%; p = 0.127). ***Conclusions:*** Increased BMI poses a greater challenge for surgical interventions such as radical cystectomy in bladder cancer patients. However, in our series, intra- and postoperative morbidity was not significantly elevated in OW patients. Overall survival was not reduced in OW compared to NW patients. Therefore, elevated BMI is not an exclusion criterion for radical cystectomy in bladder cancer patients.



## Introduction

Obesity has become a severe global health problem in the last decades. According to the World Health Organization (WHO), approximately 400 million adults are overweight and around 130 million adults are obese, accounting for 25–75% of the adult population in European countries. An increase in body mass index (BMI) contributes to diseases such as hypertension, coronary heart disease, stroke, diabetes mellitus, osteoporosis, cancer and psychological disorders [1]. The BMI is defined as the

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weight in kilograms divided by the height in squared meters and reflects the weight and nutritional status among individuals [2]. It does not distinguish between adipose tissue and lean body mass, but correlates well with body fat as measured by underwater weight or other techniques [3].

Recent studies have shown that obesity significantly increases the risk of developing malignancies, such as gastrointestinal, breast and kidney cancer [4–7]. The association between obesity and bladder cancer is less well defined. Few reports have been published evaluating the impact of adiposity on morbidity and mortality in patients with bladder cancer following cystectomy [8–10]. An increased mass of intraperitoneal fat may also impair surgical dissection and cause prolonged surgery time. Furthermore, a higher rate of peri- and postoperative complications in obese patients might reflect an unfavorable outcome. The aim of this retrospective study is to investigate the impact of BMI in patients with locally advanced bladder cancer undergoing radical cystectomy.

## Patients and Methods

In a retrospective study, 390 consecutive bladder cancer patients (283 men and 107 women) who underwent radical cystectomy from January 1986 to December 2004 were reviewed. BMI was calculated preoperatively according to WHO guidelines and patients were distributed into normal weight (NW, 18.5–24.9 kg/m$^2$), overweight (OW, 25.0–29.9 kg/m$^2$) and obese (≥30.0 kg/m$^2$) BMI subgroups. Different BMI subgroups were investigated according to defined criteria such as sex, type of urinary diversion (ileal conduit, ileal neobladder or others), time of surgery (min), number of intraoperative erythrocyte concentrates (1 unit = 250 ml), and overall survival time (months). TNM stages, resection status and postoperative complications within 3 months were associated to patients' BMI. Median and interquartile ranges are shown unless otherwise stated. Uni- and multivariate analyses were assessed using Mann-Whitney or Kruskal-Wallis test [11, 12]. Overall survival was calculated by Kaplan-Meier [13]. The log-rank (Mantel-Cox) test was performed to determine the association between BMI subgroups and overall survival time [14]. All p values are two-sided with significance considered at $p \leq 0.05$. Analyses were performed using the statistical Software Package for the Social Sciences, Version 13.0 (SPSS, Chicago, Ill., USA).

## Results

Of 390 patients who underwent radical cystectomy due to locally advanced bladder cancer, 107 were female and 283 male with a female:male ratio of 1:2.6. Age ranged from 31 to 87 years (median 68.0) at the time of surgery. Following radical cystectomy, 177 patients (45.4%) received ileal conduits and 164 patients (42.1%) orthotopic ileal neobladders. Other forms of urinary diversion such as hemi-Kock pouch, Indiana pouch, ureterocutaneostomy, ureterosigmoidostomy or colon conduit were chosen in 49 patients (12.5%). For female patients, ileal conduits were preferentially chosen compared to orthotopic neobladders (69.2 vs. 15.9%), whereas men more likely received ileal neobladders than ileal conduits (51.9 vs. 36.4%). Patients with an ileal conduit were significantly older than patients with orthotopic ileal neobladder (74.0 vs. 65.0 years; $p < 0.001$). While almost 60% of patients who received ileal neobladders showed organ-confined disease (pTis-pT2b pN0 cM0), patients with ileal conduit displayed more advanced disease (table 1).

According to WHO criteria, 178 patients (45.6%) were NW, 173 patients (44.4%) were OW, and 39 patients (10.0%) showed obesity. Mean BMI of the whole patient collective was 25.3 kg/m$^2$. The female subgroup displayed a mean BMI of 23.8 kg/m$^2$ and the male subgroup a mean BMI of 25.9 kg/m$^2$, respectively (fig. 1).

Ileal conduit was chosen in 51.1% of NW patients whereas ileal neobladder was the preferred type of urinary diversion in OW patients. Male patients were significantly younger than female patients (67.0 vs. 70.5 years; $p < 0.001$). With a median age of 68.0 years, no significant difference in age was noted between the BMI subgroups ($p = 0.207$) (table 2).

The time of surgery for radical cystectomy was associated with the patients' weight. In the OW patient group, the time of surgery was significantly prolonged with 355 min whereas the NW group displayed 330 min ($p = 0.007$). In a subgroup analysis for patients receiving an ileal conduit, OW patients represented a time of surgery of 330 min compared to NW patients with 325 min. This difference remained insignificant ($p = 0.053$). Investigating the patient group with orthotopic neobladders, OW patients showed a mean time of surgery of 355 min whereas NW patients' surgery time was significantly reduced with 320 min ($p = 0.014$) (table 2).

The number of intraoperative transfused erythrocyte concentrate units ranged from 0 to 24. No association could be found between the BMI subgroup and blood transfusion rate. However, the type of urinary diversion affected the amount of transfused erythrocyte units. Patients with an ileal neobladder required fewer transfusion units (median 2 units, interquartile range 0–3) than patients who received ileal conduits (3 units, interquartile range 2–5) or other forms of urinary diver-

**Table 1.** Number, age and TNM subgroup distribution in urinary diversion cohorts; other forms of urinary diversions include hemi-Kock pouch, Indiana pouch, ureterocutaneostomy, ureterosigmoidostomy and colon conduit

| | Total | Ileal conduit | Ileal neobladder | Others | p value |
|---|---|---|---|---|---|
| *Number of patients* | | | | | |
| All patients | 390 (100%) | 177 (45.4%) | 164 (42.1%) | 49 (12.5%) | |
| Male | 283 (72.6%) | 103 (26.4%) | 147 (37.7%) | 33 (8.5%) | |
| Female | 107 (27.4%) | 74 (19.0%) | 17 (4.4%) | 16 (4.0%) | |
| *Age, years* | | | | | |
| All patients | 68.0 (60.25/74.0) | 74.0 (67.0/77.0) | 65.0 (58.0/70.0) | 62.0 (54.0/69.0) | <0.001[a] |
| Male | 67.0 (59.0/73.0) | 72.0 (66.5/76.0) | 65.0 (57.75/70.0) | 62.0 (54.5/69.5) | <0.001[a] |
| Female | 70.5 (64.0/77.0) | 75.0 (68.0/78.0) | 63.0 (59.0/68.5) | 61.0 (48.5/70.0) | <0.001[a] |
| p value | <0.001[b] | 0.084[b] | 0.841[b] | 0.688[b] | |
| *TNM subgroup* | | | | | |
| All patients | 177 (100%) | 164 (100%) | 49 (100%) | | |
| pTis–pT2b pN0 cM0 | 59 (33.3%) | 96 (58.5%) | 22 (44.9%) | | |
| pT3a–pT4 pN0 cM0 | 61 (34.5%) | 49 (29.9%) | 19 (38.8%) | | |
| pTis–pT4 pN+ cM0 | 57 (32.2%) | 19 (11.6%) | 8 (16.3%) | | |

Median, 25, 75 percentile and p values are shown.
[a] Comparison of patients with ileal neobladders versus ileal conduits. [b] Comparison of female vs. male patients.

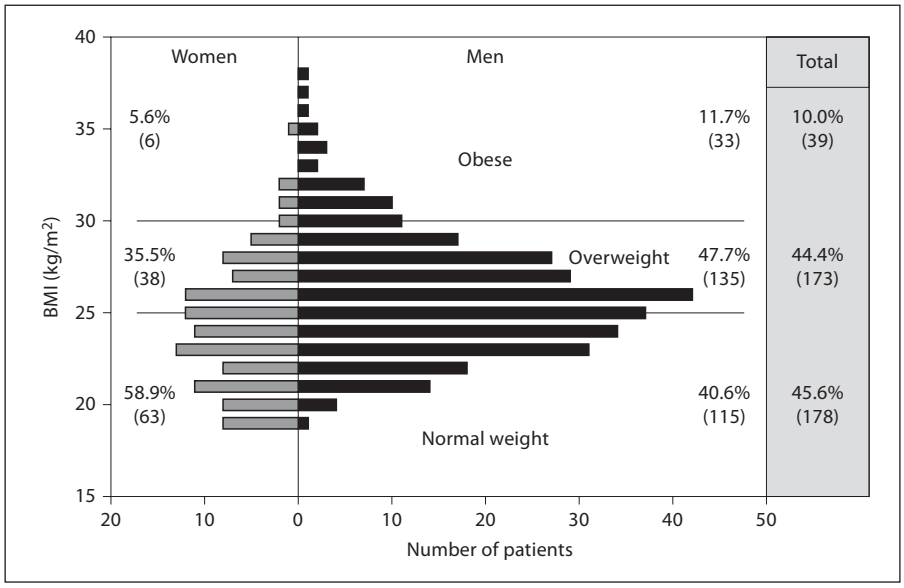


**Fig. 1.** Distribution of patients according to BMI. Percentages of BMI subgroups and absolute numbers of patients (in parentheses) are shown.

sions (3 units, interquartile range 2–4.75; $p < 0.001$) (table 2).

In 45.4% of cystectomy specimens an organ-confined bladder tumor (pTis-pT2b pN0 pM0) could be detected, whereas 33.1% of patients presented with non-organ-confined disease (pT3a–pT4 pN0 pM0) and 21.5% showed positive lymph node stage (table 2). Although the distribution of TNM subgroups in each BMI category was not identical, postoperative tumor staging revealed no significant association between BMI and pathological TNM stage.

In 64.7% of patients, complications were observed within the first 3 postoperative months. For the whole patient cohort, common complications were prolonged

**Table 2.** Age, type of urinary diversion, operation time, transfusion rate, TNM subgroup in relation to BMI group; other forms of urinary diversions include hemi-Kock pouch, Indiana pouch, ureterocutaneostomy, ureterosigmoidostomy and colon conduit

| | Total | Normal weight | Overweight | Obese | p value |
|---|---|---|---|---|---|
| *Urinary diversion* | 390 (100%) | 178 (100%) | 173 (100%) | 39 (100%) | |
| Ileum conduit | 177 (45.4%) | 91 (51.1%) | 67 (38.7%) | 19 (50.0%) | |
| Ileal neobladder | 164 (42.1%) | 58 (32.6%) | 89 (51.5%) | 17 (43.6%) | |
| Others | 49 (12.5%) | 29 (16.3%) | 17 (9.8%) | 3 (6.4%) | |
| *Age, years* | | | | | |
| All patients | 68.0 (60.25/74.0) | 69.0 (62.0/76.0) | 68.0 (60.0/74.0) | 67.0 (59.0/71.0) | 0.207[a] |
| Male | 67.0 (59.0/73.0) | 68.5 (60.0/74.0) | 67.0 (57.25/71.75) | 67.0 (59.5/71.5) | 0.508[a] |
| Female | 70.5 (64.0/77.0) | 70.0 (62.0/72.5) | 72.5 (64.5/76.0) | 67.0 (57.25/71.75) | 0.412[a] |
| p value | <0.001[b] | 0.098[b] | 0.008[b] | 0.835[b] | |
| *Operation time, min* | | | | | |
| All patients | 340 (300/410) | 330 (285/380) | 355 (300/420) | 365 (330/435) | 0.007[a] |
| Ileal conduit | 330 (292.5/392.5) | 325 (270/370) | 330 (300/420) | 370 (332.5/370) | 0.053[a] |
| Ileal neobladder | 335 (300/405) | 320 (300/370) | 355 (310/420) | 360 (317.5/427.5) | 0.014[a] |
| Others | 375 (300/450) | 372.5 (300/438.8) | 390 (285/480) | 502.5 (365/640) | 0.943[a] |
| p value | 0.356[c] | 0.617[c] | 0.570[c] | 0.598[c] | |
| *Transfusion rate, units* | | | | | |
| All patients | 2 (1/4) | 3 (2/4) | 2 (1/4) | 2 (0/3) | 0.470[a] |
| Ileal conduit | 3 (2/5) | 3 (2/5) | 3 (2/5) | 2 (0/3) | 0.541[a] |
| Ileal neobladder | 2 (0/3) | 0 (0/3) | 2 (0/3) | 2 (0/4) | 0.073[a] |
| Others | 3 (2/4.75) | 3 (2/4.75) | 3 (1.75/4.25) | 4.5 (2/7) | 0.940[a] |
| p value | <0.001[c] | <0.001[c] | <0.001[c] | 0.731[c] | |
| *TNM subgroup* | 390 (100%) | 178 (100%) | 173 (100%) | 39 (100%) | |
| pTis–pT2b pN0 cM0 | 177 (45.4%) | 74 (42.6%) | 84 (48.6%) | 19 (48.7%) | |
| pT3a–pT4 pN0 cM0 | 129 (33.1%) | 68 (38.2%) | 47 (27.2%) | 14 (35.9%) | |
| pTis–pT4 pN+ cM0 | 84 (21.5%) | 36 (20.2%) | 42 (24.2%) | 6 (15.4%) | |

Median, 25, 75 percentile and p values are shown.
[a] Comparison of normal weight versus overweight patients. [b] Comparison of male and female patients. [c] Comparison of patients with ileal neobladders versus ileal conduits.

subileus (17.0%), urinary tract infection (11.0%), thrombosis (9.5%) and prolonged wound healing (8.5%) (fig. 2). In general, in our series, patients suffering from complications did not exhibit higher BMI (25.65 kg/m$^2$, interquartile range 23.45–27.61 kg/m$^2$) than non-symptomatic patients (25.83 kg/m$^2$, interquartile range 22.83–28.01 kg/m$^2$; p = 0.67). Postoperative bleeding remained the only complication that significantly occurred more often in patients with higher BMI (30.19 kg/m$^2$, interquartile range 25.50–31.53 kg/m$^2$) than in leaner patients (25.28 kg/m$^2$, interquartile range 23.04–27.30 kg/m$^2$; p = 0.02) (fig. 2). However, perioperative mortality within 3 months of cystectomy had a tendency to be more common in patients with lower BMI (p = 0.18).

Overall survival analyses of subgroups for urinary diversion such as ileal conduit and ileal neobladder are depicted in figure 3. The estimated 5- and 10-year survival rate for OW patients who received ileal conduits was 41.1 and 29.2% and exceeded the survival rate of NW patients with 34.0 and 22.2%. However, this difference in overall survival time in this subgroup analysis remained insignificant (p = 0.140) (fig. 3a). In a subgroup analysis of patients with ileal neobladder diversion, OW patients showed a 5- and 10-year survival rate of 70.8 and 61.6%, while survival rates for NW patients were less favorable (65.1 and 53.2%). This subgroup analysis also revealed no significant differences in overall survival between OW and NW patients (p = 0.127) (fig. 3b).

When excluding patients >70 years of age at the time of radical cystectomy and analyzing patients with histological organ-confined disease (pTis–pT2b pN0 cM0),

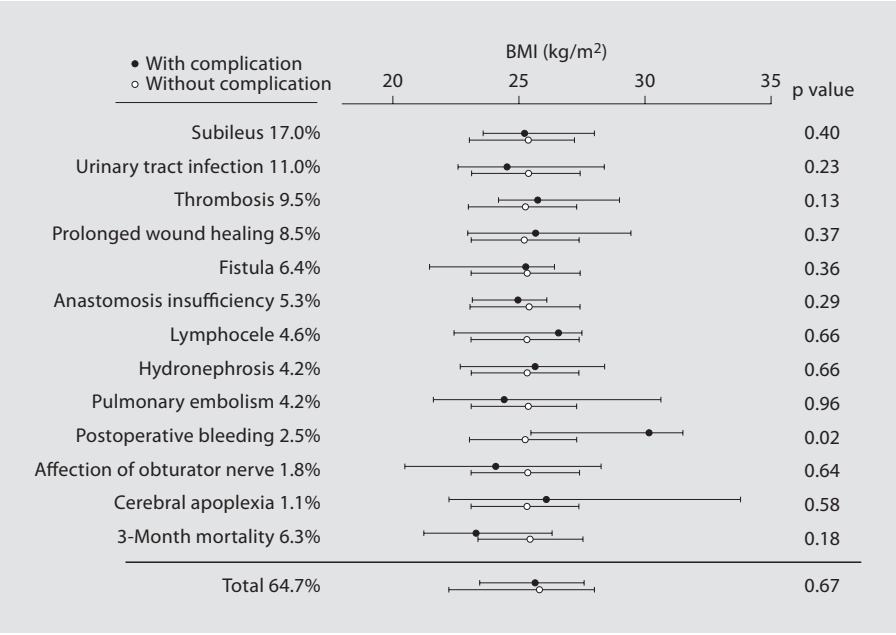


**Fig. 2.** Postoperative complications within 3 months following radical cystectomy in relation to BMI. Percentages, median, interquartile ranges and p values are shown. Filled circles indicate patients suffering from complication; empty circles represent patients without complication.

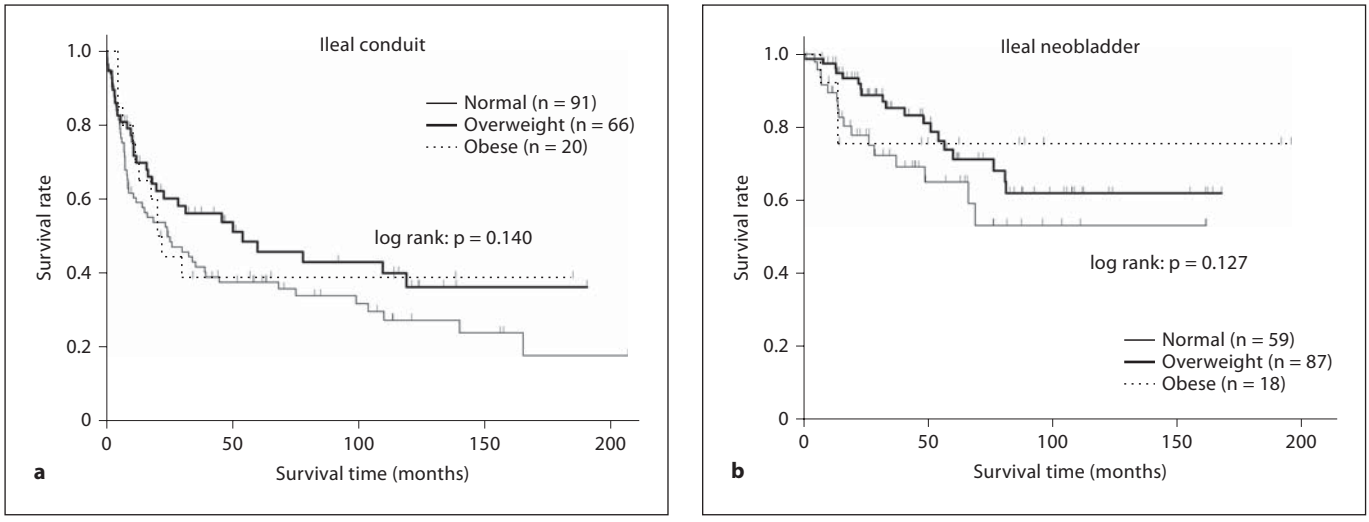


**Fig. 3.** Overall survival of patients receiving ileal conduit (**a**) or ileal neobladder (**b**) following radical cystectomy per BMI group. Kaplan-Meier analysis and result of log-rank test comparing overweight to normal weight patients are shown.

non-organ-confined disease (pT3a–pT4 pN0 cM0) or lymphatic metastases (pTis–pT4 pN+ cM0), no significant difference in overall survival could be noted between NW and OW patients (p = 0.459, p = 0.538 and p = 0.710, respectively) (fig. 4).

## Discussion

A number of studies have focused on the BMI as a risk factor for carcinogenesis. Nevertheless, only a few reports have evaluated the impact of BMI on peri- and postoperative morbidity and the outcome of bladder tumor patients following radical cystectomy [8–10]. In our study

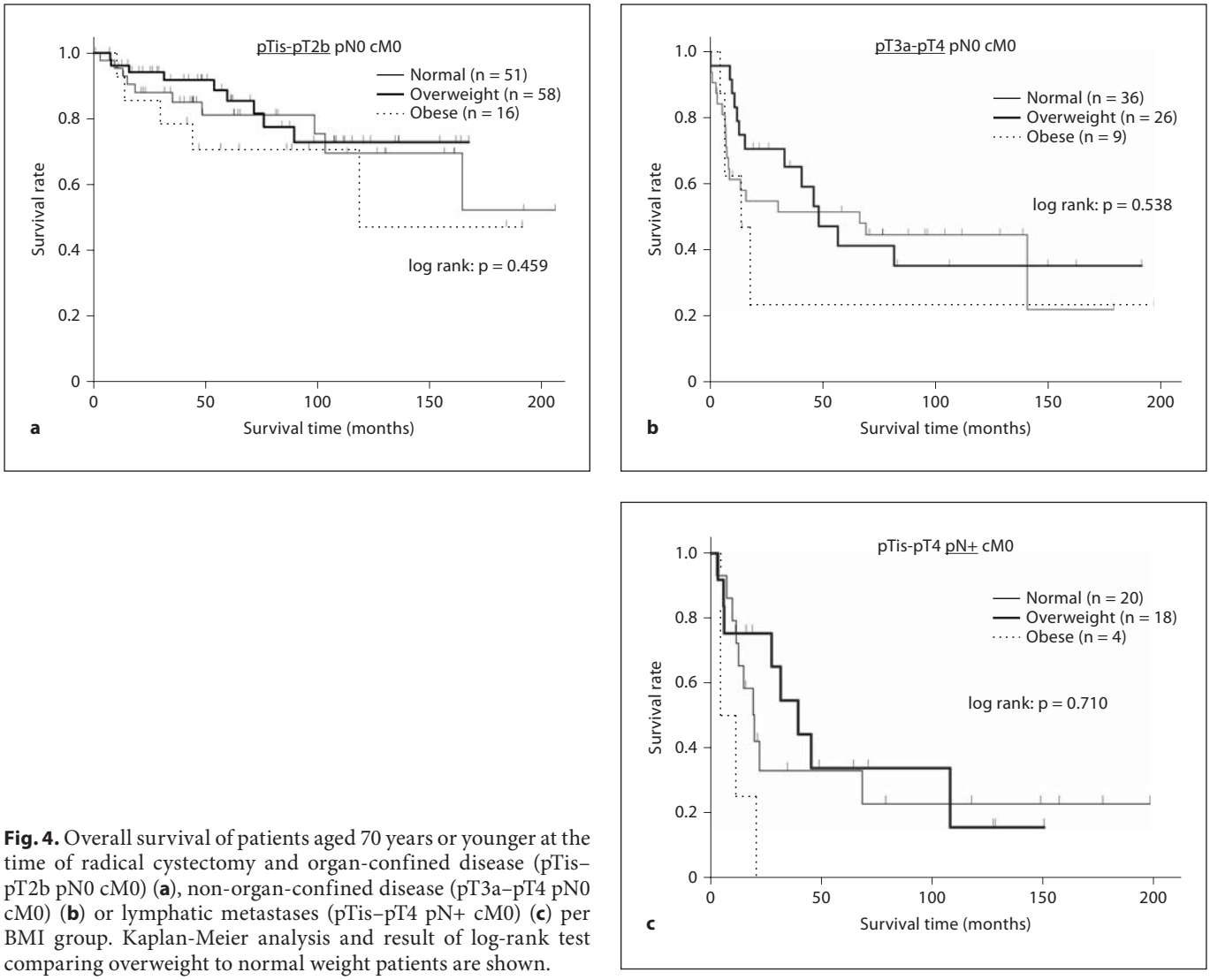


**Fig. 4.** Overall survival of patients aged 70 years or younger at the time of radical cystectomy and organ-confined disease (pTis–pT2b pN0 cM0) (**a**), non-organ-confined disease (pT3a–pT4 pN0 cM0) (**b**) or lymphatic metastases (pTis–pT4 pN+ cM0) (**c**) per BMI group. Kaplan-Meier analysis and result of log-rank test comparing overweight to normal weight patients are shown.

we observed no significant elevation of intra- and postoperative morbidity in OW patients. Increased BMI did not impair long-term survival of our bladder cancer patients following radical cystectomy. Still, increased BMI poses a greater challenge for the surgeon when performing radical cystectomy. We found a significantly prolonged time of surgery in patients with elevated BMI. In accordance with our results, a recent study by Lee et al. [9] reported an association between prolonged surgery time and the degree of obesity in bladder cancer patients. Obesity also increases operation time in patients undergoing surgery for gastric cancer [15, 16] or renal cancer [17] due to impaired surgical dissection.

Investigating the intraoperative blood loss, several reports in the field of abdominal surgery have already evaluated obesity as a severe risk factor for enhanced bleeding and blood transfusion rate [15–17]. These findings were confirmed by Lee et al. [9] for bladder cancer patients. In their study, elevated BMI was significantly associated with increased intraoperative blood loss among bladder cancer patients undergoing radical cystectomy. Another study by Chang et al. [10] analyzed preoperative parameters such as BMI, comorbidity and patient demographics in respect to blood loss for bladder tumor patients undergoing radical cystectomy. Interestingly, BMI was the only preoperative statistical parameter that could predict blood loss during radical cystectomy. In contrast to these find-

ings, we observed no significant association between BMI and enhanced blood transfusion rate during radical cystectomy. However, patients receiving ileal neobladders required fewer blood transfusions than patients receiving other forms of urinary diversion. This finding can be explained by younger age and better performance status as well as lower pathological stages resulting in lower intraoperative blood loss of patients with ileal neobladders.

Obesity may lead to higher incidence of wound infection, fascia dehiscence, subileus and postoperative lymphocele formation [9, 18, 19]. The hypothesis that obesity is a risk factor for intra- and postoperative complications remains controversial. In our series, we did not observe a higher rate of complications – except for postoperative bleeding – in patients with elevated BMI within the first 3 months following cystectomy. Similarly, Chang et al. [10] found no increased postoperative complications or longer hospital stays for obese bladder cancer patients following radical cystectomy. They concluded that overweight tumor patients do not represent a risk group for postoperative complications.

The influence of BMI on survival in bladder cancer patients is still a matter of debate as well. In our study, we noted no statistically significant difference in overall survival between NW and OW bladder cancer patients with organ-confined, non-organ-confined or lymphatic metastasized disease following radical cystectomy. Reports from Chang et al. [10] and Hafron et al. [8] observed a possible trend toward prolonged bladder cancer-specific survival in normal weight patients with organ-confined disease following radical cystectomy. However, they failed to demonstrate a significant association between BMI and bladder cancer survival time. In other malignancies such as colon carcinoma, obesity was associated with a significant increase in overall mortality [20, 21]. Contrarily, in gastrointestinal cancer as well as in urogenital tumors such as prostate and kidney cancer, survival of these patients was reported to be in favor of overweight and obese patients [22–25].

We conclude that intra- and postoperative morbidity is not significantly elevated in overweight patients and that higher BMI (up to 30 kg/m$^2$) does not impair long-term survival in bladder cancer patients following radical cystectomy. Finally, elevated BMI should not exclude patients from radical cystectomy as definitive treatment.

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