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# The Comprehensive Complication Index CCI: A proposed modification to optimize short-term complication reporting after cystectomy and urinary diversion

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## Abstract

**Objective:** To optimize complication reporting in patients undergoing cystectomy and urinary diversion (UD) using the Comprehensive Complication Index (CCI). The original CCI ranging from 0 (no complications) to 100 (death) integrates all complications weighted by severity over time in a single formula. However, due to the large number of complications after cystectomy and UD, the CCI may exceed the upper limit.

**Methods:** In an observational single-center cohort, 90-day postoperative complications in 1,313 consecutive patients undergoing cystectomy and UD from 2000 to 2017 were evaluated. Prospectively collected complications were graded according to the Clavien-Dindo classification (CDC). A modified Berne CCI was developed using an exponential function, which transforms the sum of the weights into a value between 0 and 100. The correlation between the Berne and original CCI values was depicted graphically. Finally, original CCI and Berne CCI values for each patient were extracted and compared. Predictive values of CCI scores for mortality or severe complications (CDC ≥IV) within 1 year postoperatively were investigated by use of multiple logistic regression analyses.

**Results:** Overall complication rate was 82%, with CDC grade I to II in 56% and CDC grade IIIa to V in 27% respectively. Applying the original CCI, the upper limit was exceeded in 8 patients, with a maximal value of 119.1 (median 25.7 [interquartile range: 20.9−37.2]). The maximal value of the Berne CCI was 99.4 (21.2 [14.6−39.3]) for nondeath cases. The Berne CCI predicted the onset of death and severe complications between postoperative day 91 and 365 (both $P$ <0.0001), whereas the original CCI was only predictive in interaction with other variables but not alone ($P = 0.2772$ and $P = 0.0862$, respectively).

**Conclusion:** The optimized Berne CCI depicts postoperative morbidity and burden within 90 days after cystectomy and UD without exceeding the upper index limit. It is specifically suited for longitudinal assessment of complications after cystectomy and UD taking into consideration every single complication and corresponding treatment. As the Berne CCI well predicted the onset of mortality and severe complications within 1 year postoperatively, this may allow a better preoperative patient counselling. It therefore warrants consideration for standardized reporting of complications after cystectomy and UD. 

*Keywords:* Cystectomy; Complications; Comprehensive Complication Index

## 1. Introduction

Disparity in the methodologies of gathering and reporting data, as well as the use of various and nonstandardized definitions, significantly contributes to the present discrepancies in reporting of complications [1−3]. Reproducible assessment of postoperative complications is essential for

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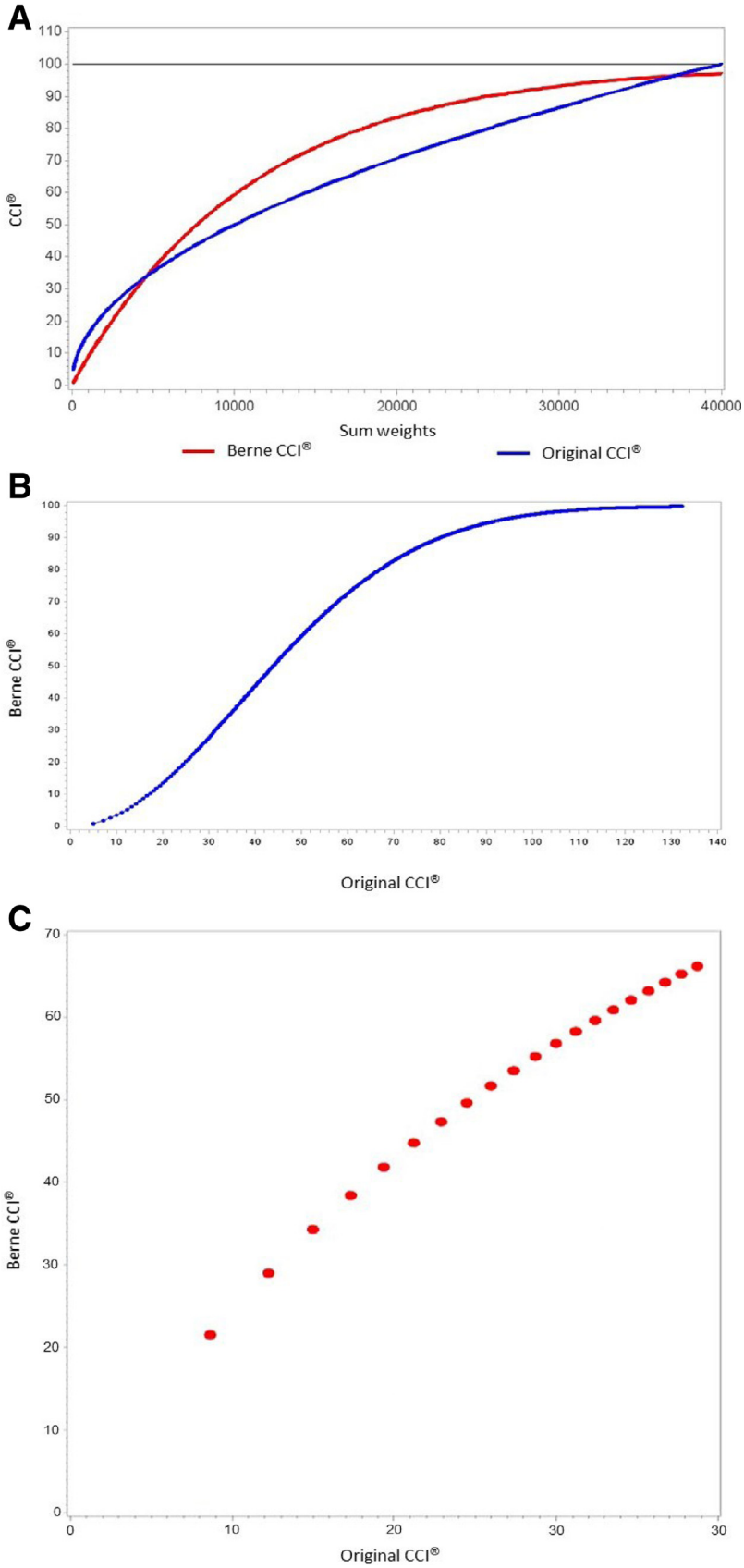


Fig. 1. (**A**): Course of curves of the Berne CCI (red line) and of the original (blue line) CCI with the gray line indicating the upper limit of 100. (**B**): Scatter plot depicting the association of the Berne (*y* axis) and original (*x* axis) CCI values. (**C**): The correlation is also shown by considering both CCI in relation to their respective numbers of Grade I complications for example. (Color version available online.)

reliable evaluation of quality of care and recovery. In an attempt to standardize the reporting of perioperative complications the Clavien-Dindo classification (CDC) was developed [4,5]. Although it is now the most frequently used classification, it only reports, however, the most severe complication of the respective patient, according to the type and degree of invasiveness of the therapy given, but it does not include less severe complications or the total number of adverse events per single patient over time. It therefore underestimates the true overall postoperative morbidity.

To improve reporting of postoperative complications, the landmark Comprehensive Complication Index (CCI) was proposed by Slankamenac et al. in 2013 [6]. It integrates all recorded complications weighted by severity into a single formula ranging from 0 (no complication) to 100 (death) [6]. Unlike the CDC, each single complication occurring during a given episode of care can easily be added to the calculation, allowing for longitudinal assessment of complications over time. This makes the CCI more sensitive than the CDC for complication reporting and also allows comparison of patients suffering from more than 1 complication [6–8]. However, in patients with multiple complications, the CCI may exceed the upper range which has been put on a level with death. This is a main limitation of the CCI when considering that death is even worse than the most imaginable number of complications a patient can suffer. The CCI was developed based on the ratings of a cohort of 227 visceral surgery patients and their physicians of the 30 most common and relevant postoperative complication scenarios at 90-day postoperative [6,9]. However, because the reference cohort was heterogeneous, including patients undergoing only minor surgery and only a minority patients who were operated on due to malignancy (33%), it is not directly comparable with a cohort undergoing cystectomy and urinary diversion (UD). Indeed, in the latter 30-day and 90-day complication rates vary between 26% to 86% and 30% to 100% [10–19] compared to 90-day rates of 25% to 54% after visceral surgery [6,8,9]. After cystectomy and UD the total number of complications, the number of patients with >1 complication, and the rate of major complications (CDC IIIa–V) can be high, resulting in a "raw" CCI sum score of >40,000, exceeding the upper limit of 100 originally defined as death.

For this reason, even though the CCI has been used successfully in several trials [20–22], we set out to optimize the original CCI formula to better summarize patient burden by setting an upper limit of 100 for any combination of complications in a single patient within 90 days after cystectomy and UD (primary outcome). In addition, we aimed to test the predictive values of this optimize CCI score for mortality or severe complications between postoperative day 91 and 365 (secondary outcome).

## 2. Patients and methods

### 2.1. Patient population and assessment of postoperative morbidity

See Appendix A [23–29].

### 2.2. Development of the modified CCI formula

The original CCI was designed by Slankamenac et al. [6] to quantify postoperative complications based on the different CDC grades. These grades were weighted according to a scale determined in an empirical study [9]. The weights of the individual complications are summed up and the CCI score is the square root of this

Table 1
Clavien-Dindo classification and the corresponding values of the Comprehensive Complication Index (CCI), adapted from Dindo et al. [4] and Slankamenac et al. [6]. Death is arbitrarily defined as a CCI score of 100.

| Grade of complication | Required intervention / therapy | Weights ($MRV_{phys} \times MRV_{pat}$) | Original CCI | Berne CCI |
|---|---|---|---|---|
| CDC I | Any deviation from normal postoperative course requiring only physiotherapy and drugs as follows: antiemetics, antipyretics, diuretics, electrolytes, prokinetics | 300 | 8.7 | 2.7 |
| CDC II | Pharmacological treatment (with drugs other than required for CDC I complications), blood transfusion, total parenteral nutrition | 1,750 | 20.9 | 14.6 |
| CDC IIIa | Surgical, endoscopic or radiological intervention not under general anaesthesia | 2,750 | 26.2 | 21.9 |
| CDC IIIb | Surgical, endoscopic or radiological intervention under general anaesthesia | 4,550 | 33.7 | 33.6 |
| CDC IVa | Single-organ dysfunction requiring intermediate or intensive care unit management | 7,200 | 42.4 | 47.7 |
| CDC IVb | Multiorgan dysfunction requiring intermediate or intensive care unit management | 8,550 | 46.2 | 53.7 |
| CDC V | Death | – | 100 | 100 |

CDC = Clavien-Dindo classification; MRV = median referrence value.

Table 2
Baseline, surgical, and oncological characteristics of 1,313 patients undergoing cystectomy and urinary diversion.

| | $N = 1,313$ |
|---|---|
| **Age (y)** | 68.4 (60.6–75.5) |
| Gender, n (%) | |
| male | 871 (66) |
| female | 442 (34) |
| ASA classification | |
| 1 | 33 (3) |
| 2 | 683 (52) |
| 3 | 569 (43) |
| 4 | 28 (2) |
| Body mass index (kg/m$^2$) | 25.6 (22.9–28.7) |
| Charlson comorbidity index >2 | 373 (28) |
| Diabetes mellitus | 180 (14) |
| Smokers | 728 (55) |
| Antihypertensives | 573 (44) |
| Beta blockers | 269 (20) |
| Statins | 278 (21) |
| Renal function, eGFR [ml/min] | |
| >90 | 355 (27) |
| [60–90] | 565 (43) |
| [30–60] | 333 (25) |
| <30 | 60 (5) |
| Preoperative anemia | 531 (40) |
| Glasgow prognostic score | |
| 0 | 501 (38) |
| 1 | 556 (42) |
| 2 | 256 (19) |
| Neoadjuvant chemotherapy | 176 (13) |
| Adjuvant/palliative chemotherapy (≤90 d) | 61 (5) |
| Adjuvant/palliative radiochemotherapy (≤90 d) | 12 (1) |
| Early abdominal surgery | 539 (41) |
| Surgical parameters | |
| Duration of surgery (min) | 390 (345–432) |
| Intraoperative blood loss (ml) | 1,000 (700–1,500) |
| Urinary diversion | |
| Orthotopic ileal bladder substitute | 592 (45) |
| Ileal conduit | 592 (45) |
| Ileal catheterisable pouch | 105 (8) |
| Ureterocutaneostomy | 21 (2) |
| Ureterosigmoidostomy | 3 (1) |
| Oncological parameters (n = 1,183) | |
| Pathologic stage | |
| ≤T1 | 323 (27) |
| T2 | 315 (27) |
| T3 | 409 (35) |
| T4 | 136 (11) |
| Nodal stage | |
| N0 | 861 (73) |
| N+ | 322 (27) |
| Number of lymph nodes removed | 32 (21–44) |
| Length of hospital stay (d) | 17 (15–21) |
| Readmission rate (≤90 d) | 358 (27) |
| Time interval (d) between TUR-B and radical surgery (patients with neoadjuvant chemotherapy excluded) | 47 (28–84) |

ASA = American Society of Anesthesiologists; eGFR = estimated glomerular filtration rate; TUR-B = transurethral resection of the bladder.

Anemia was defined according to the World Health Organization recommendation: hemoglobin <130 g/l for men and <120 g/l for women. Data are reported as median (interquartile range) or frequency (%).

sum divided by 2, where $MRV_{phys}$ and $MRV_{pat}$ are the median reference values of physicians (phys) and patients (pat), yielding the formula [6,9]:

$$\text{Original CCI} = \sqrt{\left(\sum MRV_{phys} \times MRV_{pat}\right)}/2$$

In the case of death, the CCI score is put at 100. With several severe complications or numerous moderate complications without death, the score in the original CCI may be >100 [6]. This should not happen because death as the worst event should have the highest possible CCI value. Furthermore, an index as a reference value should not exceed 100 from a mathematical point of view.

We therefore set out to modify the CCI to eliminate this drawback while retaining Slankamenac et al.'s concept of summing up all the weights of complications occurring in a patient [6]. The formula of Slankamenac et al. was developed in relation to a normal distribution [6], but an index with a value of 100 for the event "death" has no relation to normal distribution. Index values are typically not distributed normally, due to the boundaries of 0 and 100. The index should be related to the probability of a severe event or death.

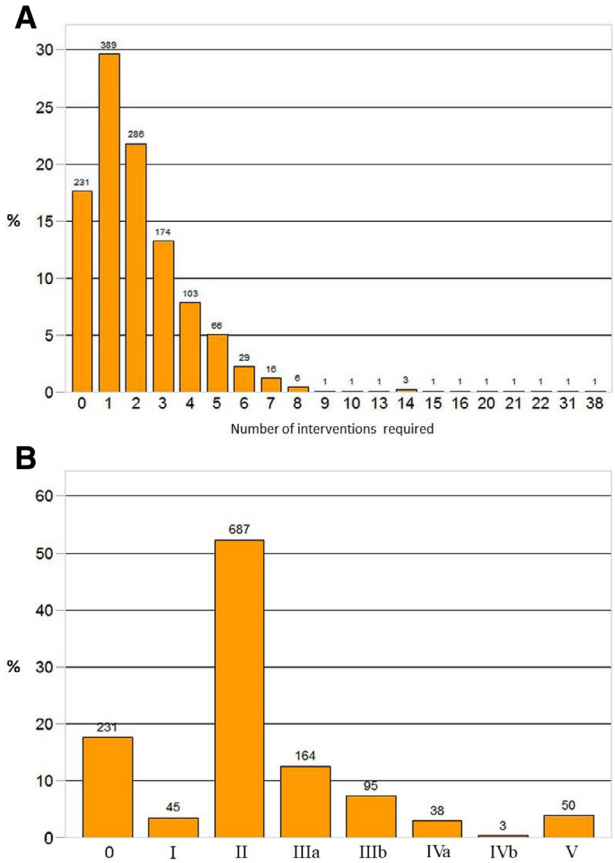


Fig. 2. (**A**): Frequency of patients who underwent each of the different numbers of interventions. (**B**): Frequency of patients with various CDC grades. The highest grade for a given patient was used.

The probability of such an event is often captured with a logistic regression model. However, the logistic function depends on a continuous argument from −infinity to +infinity. Due to the use of positive weights, only the positive part of the argument is used. This can be further simplified by use of the exponential function, 100*(1−exp(−$a$*$x$)), which transforms the sum of the weights $x$ into a value between 0 and 100.

Instead of the logistic or the exponential function, any other increasing function bounded by 0 and 100 that does not reach 100 for any positive argument can be used. In case of death the value is set at 100. The setting implies that such an index is never larger than 100. We prefer the exponential function because of its relationship to the mentioned logistic regression.

The modified CCI should be defined so that minor complications are allotted a small CCI value, severe complication or multiple moderate complications a larger value. For several severe complications, the value should approach but not exceed 100. Furthermore, the modified CCI ought to resemble the original CCI. To achieve this aim, we adapted the original CCI by applying different possible parameters "a" in the formula. The parameter "a" was based on the maximum distance between the original and the modified CCI (i.e. called Berne CCI) functions between maximum "raw" CCI sum scores ranging from 0 to 40,000, 50,000, or 60,000, resulting in the red curve on Fig. 1A. The value "a" was chosen as the smallest maximal distance between the 2 CCI functions, and based on an excellent correlation between the original CCI and the Berne CCI using our data set.

To achieve this in our cohort, we took into consideration that CDC grade I and II complications requiring interventions (e.g. electrolyte substitution, oxygen administration, and regular bedside vaccum assisted closure-therapy (VAC) dressing change) are much more common than complications requiring admission to intermediate or intensive care units. To prevent overestimation of burden, our modified CCI formula weights single minor CDC complications lower than higher grade complications while still strong correlating with the original CCI values. The CCI values of higher grade single CDC complications were adjusted accordingly to prevent underestimation of burden (Fig. 1B and C, Table 1).

In accordance with the distribution of the most frequent and relevant complications and to satisfy our aim, using the above-mentioned criteria, we chose $a = 0.00009$, resulting in the formula:

$$\text{Berne CCI} = 100 * \left(1 - \exp\left(-0.00009 * \sum \left(\text{MRV}_{\text{phys}} \times \text{MRV}_{\text{pat}}\right)\right)\right)$$

The value "$a = 0.00009$" showed an excellent correlation between the original CCI and the Berne CCI ($r = 0.9754$). This formula has several improvements over the original CCI (Fig. 1A). First, it never exceeds 100 and only equals 100 in case of death. Second, for several severe complications it can almost reach 100. Third, the formula produces higher values for severe and lower values for minor complications, allowing a more adequate discrimination of the degree of severity of complications.

We investigated predictive values of CCI scores for mortality or severe complications between postoperative

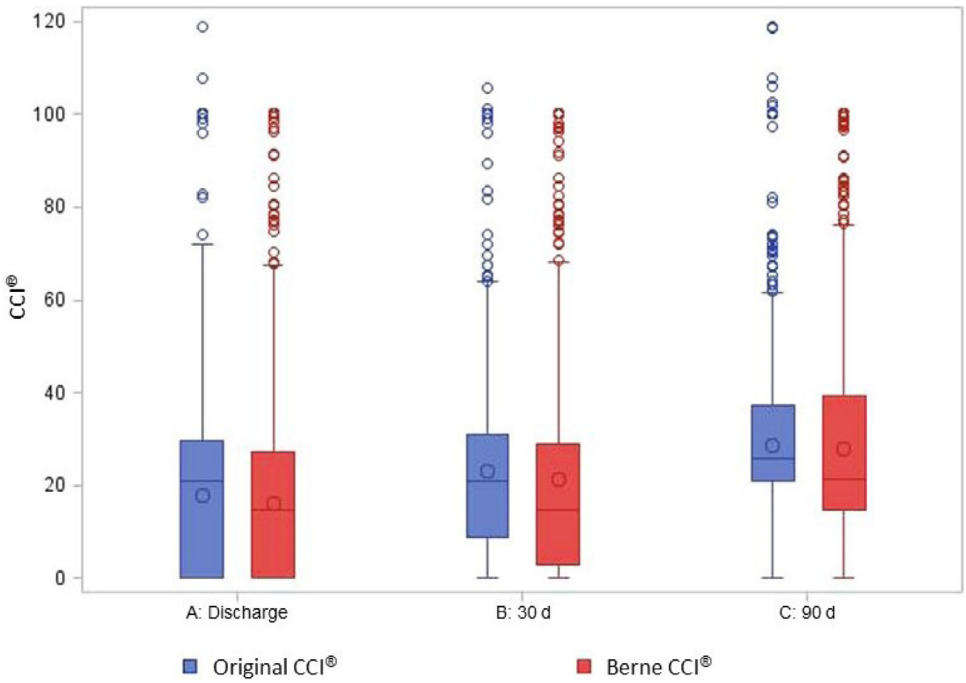


Fig. 3. (**A**): Box whisker plots (including mean) of Berne and original CCI at discharge, and (**B**): at 30-day and (**C**): at 90-day postoperatively. Multiple values are not indicated in these plots.

day 91 and 365 using a logistic regression analyses. The models included all relevant variables: age, UD, pelvic lymph node dissection, ASA score, Charlson comorbidity score, body mass index, length of stay, readmission rate and the total number of complications, maximum CDC, and one of the CCI score per patients within 90 days post-operative. We aimed to depict if the original CCI and/or the Berne CCI were relevant predictors for mortality and onset of severe complication (i.e. CDC >3) between post-operative day 91 and 365. The models were selected by a backward selection starting also with all possible 2-factor interactions. Each CCI was separately analyzed in the model. Receiver-Operating-Characteristic areas under the curve (ROC-AUC) were calculated for accuracy for each model.

## 3. Results

Baseline, surgical, and oncological characteristics of the 1,313 patients analyzed in this study are listed in Table 2.

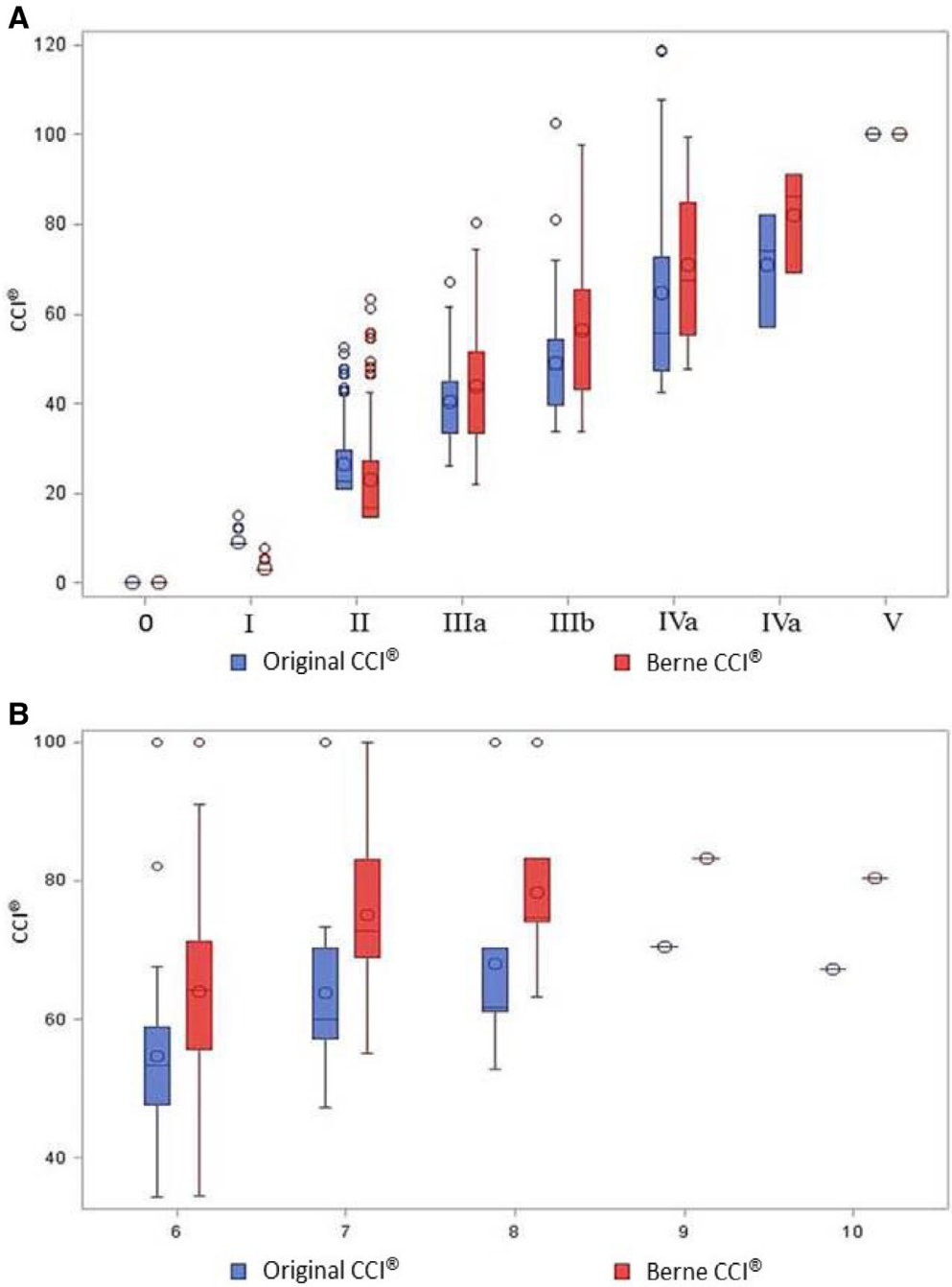


Fig. 4. Box whisker plots (including mean) of Berne and original CCI for the (**A**) various complication grades with the highest CDC grade for a given patient and (**B**) for patients with 6–10 complications.

### 3.1. Frequency and severity of complications

At least 1 CDC complication occurred in 1,082/1,313 patients (82%). Of these, 389/1,313 patients (30%) required only 1 intervention, 130/1,313 patients (10%) more than 4 interventions. More than 10 complications were observed in 11/1,313 patients (1%), nearly all of whom suffered from wound healing disorders requiring repeated bedside VAC dressing changes (Fig. 2A).

Minor CDC complications occurred in 732/1,313 patients (56%), major complications in 350/1,313 (27%). The median number of complications in patients with CDC grade IV was 4 (interquartile range : 2–6). Most complications were CDC grade II (e.g., blood transfusions, and total parenteral nutrition), observed in 687/1,313 patients (52%). Intermediate or intensive care was required for 41/1,313 patients (3%). The 90-day mortality was 3.8% (50/1,313) (Fig. 2B).

### 3.2. Values and distribution of the CCI

In patients experiencing complications, the median Berne CCI score was 14.6 (0–27.0) at discharge, 14.6 (2.7–28.0) at 30-day and 21.2 (14.6–39.3) at 90-day. The median original CCI score was 20.9 (0–29.6) at discharge, 20.9 (8.7–30.8) at 30-day and 25.7 (20.9–37.2) at 90-day (Fig. 3). The median Berne and original CCI scores for various complication grades are shown in Fig. 4.

Because a majority of patients developed only 1 or 2, mainly CDC grade II complications, which have Berne and original CCI scores of 14.6 and 20.9 respectively, a spike in both CCI can be observed between 10 to 20 and 20 to 30, respectively. Applying the Berne CCI, the maximal possible index score is 99.4. By contrast, the original CCI score exceeded 100 in 8/1,313 patient (0.6%), with a maximal index score of 119.1, indicating a complication worse than death (Fig. 5). Appendix B: Examples of clinical situations and resultant Berne and original CCI® scores.

### 3.3. Predictive values of CCI scores for mortality or severe complications within 1 year postoperatively

The Berne CCI significantly predicted the onset of death between POD 91 and 365 (maximum likelihood estimates 0.0546 ± SD 0.0129, $P$ <0.0001; Table 3). The original CCI predicted the onset of death only in interaction with the total number of complications but not alone (maximum likelihood estimates −0.0071 ± SD 0.0065, $P = 0.2772$). The number of death within this period was 152/1,149. The Berne CCI was also a significant predictor for the onset of severe complication (CDC IV and V) with a maximum likelihood estimate of 0.0603 (±SD 0.0126, $P$ <0.0001). The original CCI only predicted in interaction with pelvic lymph node dissection and maximum CDC but not alone (−0.1130 ± SD 0.0659, $P = 0.086$). The number of CDC ≥ IV within this period was 156/1,145.

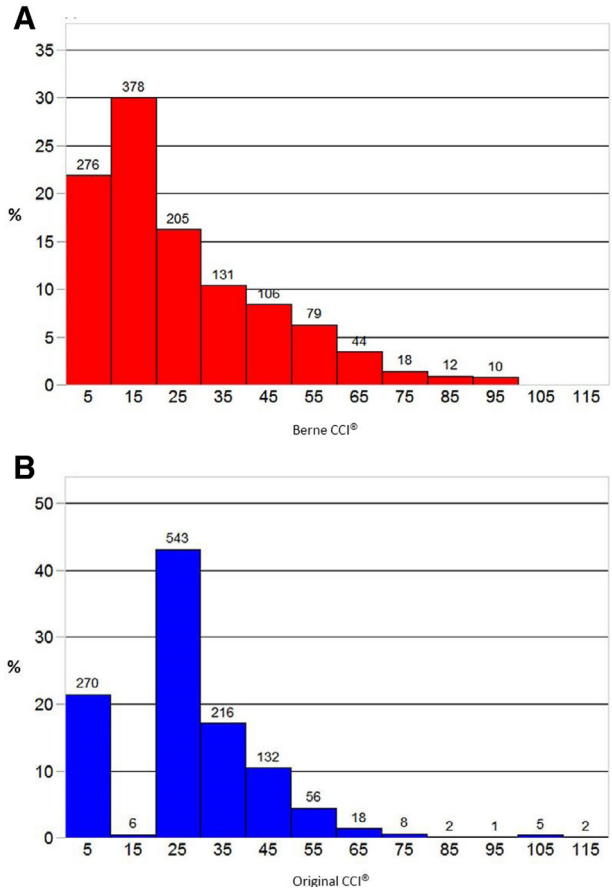


Fig. 5. Frequency distribution of Berne (**A**) and original (**B**) CCI of the 1,313 patients without complications and with CDC I–IVb complications. Death, which is arbitrarily defined with a CCI score of 100, is excluded to bring the threshold value of 100 for survivors into prominence.

## 4. Discussion

The modified Berne CCI presented here summarizes all complications after cystectomy and UD in a single formula with a fixed upper limit of 100 (which by definition means death). This contrasts with the original CCI, where multiple complications can produce a score >100. Furthermore, our formula estimates the burden of complications specifically occurring after cystectomy and UD. Hence our optimized formula depicts more accurately than the original CCI the entire spectrum of postoperative morbidity in patients with >1 complication within 90 days after cystectomy and UD. In addition, the Berne CCI could significantly predict the onset of death or severe complications in the period between postoperative day 91 and 365.

If the original CCI is applied by integrating every single complication occurring within 90 days postoperatively, 0.6% of patients would have a raw sum score >40,000 and hence an original CCI score >100 with a maximal score of 119, far exceeding the 100 set for death. Such scores were found in 1/227 patients (0.4%; maximal original CCI 102) of the reference cohort [9] and in 1/1,255 patients (0.08%) of another cohort undergoing major visceral surgery [6].

Table 3
Multiple logistic regression analyses for mortality and severe complications (CDC ≥IV) between postoperative day 91 and 365. Berne and original CCI were separately analyzed in the models.

| Variables | Max. likelihood estimates | Standard error | *P* value |
|---|---|---|---|
| **A: mortality between POD 91 and 365** | | | |
| *Original CCI* | | | |
| Urinary derivation | | | |
| OBS | −0.342 | 0.169 | 0.044 |
| IC | −0.234 | 0.260 | 0.368 |
| PLND | −0.477 | 0.195 | 0.014 |
| LOS | 0.025 | 0.009 | 0.008 |
| ∑complications | 0.540 | 0.123 | <0.0001 |
| Original CCI | −0.007 | 0.007 | 0.277 |
| Original CCI × ∑complications | −0.005 | 0.001 | <0.0001 |
| *Berne CCI* | | | |
| Urinary derivation | | | |
| OBS | −0.338 | 0.170 | 0.046 |
| IC | −0.261 | 0.261 | 0.318 |
| PLND | −0.480 | 0.195 | 0.014 |
| LOS | 0.022 | 0.009 | 0.018 |
| CDC | 0.012 | 0.017 | 0.477 |
| Berne CCI | 0.054 | 0.013 | <0.0001 |
| Berne CCI × CDC | −0.001 | 0.0003 | <0.0001 |
| **B: severe complications between POD 91 and 365** | | | |
| *Original CCI* | | | |
| Urinary derivation | | | |
| OBS | −0.369 | 0.167 | 0.027 |
| IC | −0.197 | 0.251 | 0.432 |
| PLND | −0.658 | 0.496 | 0.185 |
| BMI | −0.042 | 0.020 | 0.042 |
| LOS | 0.025 | 0.009 | 0.009 |
| ∑complications | 0.958 | 0.336 | 0.004 |
| Original CCI | −0.113 | 0.066 | 0.086 |
| Original CCI × PLND | −0.162 | 0.064 | 0.012 |
| ∑complications × PLND | 0.916 | 0.336 | 0.006 |
| CDC | 0.148 | 0.058 | 0.010 |
| CDC × PLND | 0.128 | 0.057 | 0.026 |
| Original CCI × CDC | −0.001 | 0.0003 | 0.0002 |
| *Berne CCI* | | | |
| Urinary derivation | | | |
| OBS | −0.243 | 0.163 | 0136 |
| IC | −0.401 | 0.248 | 0.107 |
| BMI | −0.041 | 0.020 | 0.040 |
| LOS | 0.024 | 0.009 | 0.008 |
| CDC | 0.001 | 0.017 | 0.554 |
| Berne CCI | 0.060 | 0.013 | <0.0001 |
| Berne CCI × CDC | −0.001 | 0.0003 | <0.0001 |

BMI = body mass index; CDC = Clavien-Dindo classification; IC = ileum conduit; LOS = length of stay; OBS = orthotopic bladder substitute; PLND = pelvic lymph node dissection; POD = postoperative day; ∑complications = total number of complications.

The ROC-AUC for the model for mortality between POD 91 and 365 was 0.6921. The urinary diversion ureterocutaneostomy and ureterosigmoidostomy ($n = 24$) were excluded of the analysis due to the low number of events; the ROC-AUC for the model for the onset of death in the interaction with the total number of complications was ROC-AUC 0.6961; the ROC-AUC for the model for the onset of severe complication (CDC IV and V) was 0.6949; the ROC-AUC for the model for the interaction with PLND and maximum CDC was ROC-AUC 0.7070.

The inability to adequately represents multiple complications (also over time during follow-up) and the different and heterogeneous populations used to establish the index underscore the need for an optimized CCI. Moreover, our formula incorporates the mathematical principle of an index value being a reference value between 0 and 100 in order to make morbidity comparable between different patients.

There are several reasons for the higher "raw" CCI sum score in patients after cystectomy and UD vs. the visceral surgery used to develop the original formula. First, the overall complication rate after cystectomy and UD was 82%, markedly higher than that of the reference cohorts [8,9]. This may be because the minor and major interventions commonly performed after visceral surgery are associated with fewer and less severe complications.

Furthermore, malignant disease was the indication for cystectomy and UD in the vast majority of our cohort, predisposing the individual patient to a higher risk of multiple and more severe complications. In our series, for example, 31% of our patients developed at least 2 complications, compared to 8% in the reference cohort [8]. Moreover, our patients with higher-grade CDC complications also had a higher number of complications.

Second, compared to the reference cohort [9], our patients were highly comorbid (American Society of Anesthesiologists score of 3–4 in 45%), hence they had a greater risk of a complex postoperative course due to the lack of functional reserve.

Third, according to the consensus on the 5 difficult complication scenarios described by Clavien et al. [8], complications requiring repeated interventions to achieve complete healing (e.g., anastomotic stricture, nipple stenosis, urinary tract infection, and metabolic acidosis) count as 2 or more complications. One complication requiring repeated interventions (e.g., stepwise transurethral resection of mucosal prolapse to avoid causing urinary incontinence) was counted as multiple complications.

Applying the optimized Berne CCI formula at different time points postoperatively enables precise longitudinal measurement of morbidity after cystectomy and UD. Furthermore, it allows identification of modifiable factors to obtain an exact assessment of surgical success, improve surgical technique and patient management and to reduce overall complication rates after cystectomy and UD. However, it is of great importance to be able to appreciate higher CCI scores and to do not overestimate the apparent severity in selected cases. Finally, the Berne CCI was a significant predictor for mortality and severe complication in the period between postoperative day 91 and 365. This observation is of importance in term of patients counselling and follow-up.

Our modification is not without limitations. Our formula, for instance, is based on best approximation of the original CCI within a fixed limit sum weight value (50,000) and on the exponential function. In addition, it does not take preoperative morbidity into account. Our optimized formula needs further external validation in other cohorts.

## 5. Conclusion

The optimized Berne CCI well depicts postoperative morbidity and burden in patients with > 1 complication within 90 days after cystectomy and UD and was a good predictor of mortality and severe complications thereafter within 1 year. It is specifically suited for longitudinal assessment of complications after cystectomy and UD taking into consideration every single complications and its corresponding treatment and may therefore allow better preoperative patient counselling before the intervention is considered. It therefore warrants consideration for standardized reporting of complications after cystectomy and UD.

## Conflict of interest

The authors declare no conflicts of interest.

## Supplementary materials

Supplementary material associated with this article can be found, in the online version, at https://doi.org/10.1016/j.urolonc.2018.12.013.

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