



# Which tool is the best for grading overall postoperative morbidity following esophagectomy?

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Esophageal cancer management by esophagectomy is associated with significant risks since esophagectomy is a major procedure. Postoperative complications following esophagectomy can range from a simple urinary tract infection to something as severe as an anastomotic leak requiring intensive care unit (ICU) admission. Post esophagectomy mortality has significantly decreased over the past years (1,2). Evaluation of overall health status following esophagectomy is essential to assess quality of esophagectomy. The Comprehensive Complication Index (CCI) is a novel tool for assessment of overall morbidity postoperatively (3). In contrast with the Clavien-Dindo Classification (CDC), CCI considers the severity of each complication that happened postoperatively. In addition, each complication is graded separately in accordance with the CDC severity classes. Then the CCI can be calculated by the summation of all CDC severity classes thought a formula, which was developed by utilizing an adopted operating-risk-index. This formula is embedded in an automated CCI calculator that can be found easily online.

We congratulate Mathes and their colleagues for publishing their important work “Comparison of the Comprehensive Complication Index and Clavien-Dindo Classification for Grading of Postoperative Complications After Ivor-Lewis Esophagectomy in a High-Volume Center” (4). The authors concluded that the correlation

between length of stay (LOS) and CCI is significantly stronger than the correlation between LOS and CDC, even when there are no major complications. This conclusion is consistent with similar studies in the literature.

A nationwide study using data on esophagectomies available through the Dutch upper gastrointestinal cancer audit (DUCA) (2,396 patients) (3); found that complicated postoperative course at the inpatient level was strongly correlated with 75th percentile of CCI outcome. However, the same study showed that no correlation was observed with CDC grade  $\geq$ III complication. In addition, a study comparing open (193 patients) versus minimally invasive esophagectomy (190 patients) for esophageal cancer by Carroll *et al.* 2020 (5), found that CCI correlates strongly with the CDC. Furthermore, positive correlation was observed between LOS and both CDC grade and CCI ( $r=0.58$  and  $0.60$ , respectively), respectively. A study of 621 patients by Slaman *et al.* 2015 (6), found strong correlation between CDC and LOS ( $r=0.65$ ), ICU-LOS ( $r=0.52$ ), and reintubation rate ( $r=0.52$ ). In addition, moderate correlation was found between CDC and prolonged LOS ( $r=0.53$ ), prolonged ICU-LOS ( $r=0.49$ ), re-intervention ( $r=0.42$ ) and re-operation rate ( $r=0.47$ ). In comparison with CDC, significantly stronger correlation was observed between CCI and LOS, prolonged LOS, reintervention, and reoperation rate. However, CCI correlations with reintubation and

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prolonged ICU-LOS, were not significantly different from the correlations with CDC. Likewise, Ma *et al.* 2018 study (144 patients) showed a significantly stronger correlation between CCI and in-hospital charge than between CDC and in-hospital charge. The correlation of in-hospital charge with CCI is significantly stronger than with CDC ( $r=0.639$  and  $0.578$ , respectively) (7). A study of 229 patients by Kudo *et al.* 2022 (8); categorized patients using receiver-operating characteristics (ROC) curve analysis into 2 groups, a group with values of  $CCI \geq 33.7$  (CCI-high group) and a group with CCI values of  $<33.7$  (CCI-low group). No significant differences were observed between the two groups regarding clinicopathological factors such as gender, age, tumor site, tumor invasion depth, metastasis to lymph nodes, and neoadjuvant chemotherapy. The rate of intraoperative transfusion in the CCI-high group was significantly greater than in the CCI-low group. The rate of 5-year overall survival was significantly less in the CCI-high group (49.5%) than in the CCI-low group (65.7%).

In contrast with the above studies, it seems that what applies to esophagectomy doesn't apply to other abdominal surgeries. Ray *et al.* 2019 (9) found no statistically significant difference when comparing between CDC and CCI; in regards to strength of correlation with outcomes (spearman's correlation testing) and prediction accuracy of outcomes (linear regression testing). The studied patients included patients who underwent hepato-pancreato-biliary, colorectal, or other abdominal surgeries. Following Spearman's correlation testing, both CDC and CCI showed significant correlation with LOS ( $r=0.580$  and  $0.577$ , respectively), ICU-LOS ( $r=0.623$  and  $0.618$ , respectively), and time to normal activity ( $r=0.46$  and  $0.49$ , respectively). Subgroup analysis for patients according to urgency of management was done, emergency and elective operations were 212 and 788, respectively. Similar correlation was observed between both CCI and CDC with the outcome variables. Another subgroup analysis was done according to the mode of surgery, patients undergoing surgery by the open route and the laparoscopic route were 877 and 123, respectively. Following linear regression, no significant difference in correlation was observed between both CCI and CDC with the outcome variables, both CDC and CCI had a statistically significant correlation in terms of predictability with LOS ( $r^2=0.408$  and  $0.404$ , respectively), and time to normal activity ( $r^2=0.21$  and  $0.22$ , respectively). The data were stratified in accordance with major complications ( $CDC \geq III$  and  $CCI \geq 30$ ) and minor complications ( $CDC < III$  and  $CCI < 30$ ), to compare the

accuracy of prediction of CDC and CCI. Comparison showed that CDC and CCI have good accuracy in the prediction of LOS [area under the curve (AUC)  $0.906$  and  $0.890$ , respectively], ICU-LOS (AUC  $0.874$  and  $0.851$ , respectively), and time to normal activity (AUC  $0.771$  and  $0.762$ , respectively). Although difference was small and statistically insignificant, CDC showed relatively greater predictive accuracy than CCI in predicting LOS, ICU-LOS, and time to normal activity. Therefore, CCI needs to be investigated in other surgical fields, because it might not be as strong as in the esophagectomy arena.

The Complication Severity Score (CSS) was invented in 2015. Similar to CCI, CSS is based on CDC and has an overall score from zero to 100 (10). It is worth mentioning that the publication of this scale was rejected initially (10), then was published in 2018 (11). The authors claim that it is better than CCI, as CCI assigns inappropriately greater score to a combination of complications. Putting it in an example, a patient who has two CDC grade II complications gets a greater CCI score than a patient who has a single CDC grade IIIa complication (11). Thus, the CSS is close to the CCI in regards to elaboration and formula, but the difference that it assigns smaller weight to each CDC grade (12). We hope that further studies on this metric would be published soon.

In conclusion, all studies reported stronger correlation for the CCI with the different postoperative outcomes following esophagectomy when compared to the CDC. Even though calculating CCI scores can be seen as more complex and more time consuming when compared to CDC, CCI seems to be a potentially useful severity scoring system for evaluation of complications and thus for prediction of outcomes. In addition, CCI might have the potential to be used in comparing postoperative morbidity between arms of future randomized controlled trials (RCTs), in a more accurate fashion than the CDC. However, we encourage the usage of both CDC and CCI when reporting postoperative complications and morbidity, to promote more comparative studies, thus adding studies of stronger quality to give CCI more validity. In addition, CCI utility in costs analysis is an area that should be investigated. The transparent recording of complications postoperatively is a scientific and ethical obligation. With the CCI system, there are enough ways to record complications with high level of both accuracy and efficiency. The power of the data gather could have far lasting implications in healthcare if unitized broadly and monitored at the national level.

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