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ΔΙΠΛΩΜΑΤΙΚΗ ΕΡΓΑΣΙΑ

Επικύρωση της καμπύλης εκμάθησης στην λαπαροσκοπική χειρουργική του παχέος εντέρου και του ορθού με τη εφαρμογή σημειακής ανάλυσης: η εμπειρία μέσα από ένα μη δομημένο σύστημα εκπαίδευσης

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Change point analysis validation of the learning curve in laparoscopic colorectal surgery: experience from a non-structured training setting

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Θα ήθελα να ευχαριστήσω τα μέλη της τριμελούς επιτροπής για την συμβολή και την στήριξη στην ολοκλήρωση της παρούσας ερευνητικής εργασίας.

Περίληψη

Σκοπός

Στην παρούσα εργασία παρουσιάζεται η εμπειρία μας σχετικά με την καμπύλη εκμάθησης της λαπαροσκοπικής κολο-ορθικής χειρουργικής, μέσα από ένα μη δομημένο περιβάλλον εκπαίδευσης.

Μέθοδοι

Πραγματοποιήθηκε αναδρομική ανάλυση μιας προοπτικής βάσης δεδομένων από το τριτοβάθμιο ίδρυμά μας. Η χειρουργική ομάδα αποτελούνταν από δύο χειρουργούς χωρίς προηγούμενη έκθεση στις λαπαροσκοπικές κολο-ορθικές επεμβάσεις (LCRO). Σε περίπτωση κακοήθειας, εφαρμόστηκαν όλες οι απαραίτητες ογκολογικές αρχές. Συμπεριλήφθηκαν όλοι οι ενήλικες ασθενείς που υπεβλήθησαν σε εκλεκτική ή ήμι-εκλεκτική λαπαροσκοπική επέμβαση παχέος εντέρου (LCO) ή ορθού (LRO). Τα διαγράμματα CUSUM που επιβεβαίωναν την ύπαρξη καμπύλης εκμάθησης, αναλύθηκαν περαιτέρω με την χρήση σημειακής ανάλυσης (CPA).

Αποτελέσματα

Συνολικά πραγματοποιήθηκαν 133 LCO και 81 LRO. Όσον αφορά τον χρόνο επέμβασης, η καμπύλη εκμάθησης στις LCRO αποτελούνταν από 3 φάσεις. Η CPA υπολόγισε την 110η επέμβαση ως το σημείο αλλαγής των δύο πρώτων φάσεων. Μετά το 145ο περιστατικό παρατηρήθηκε η ύπαρξη ενός πλατό. Περαιτέρω ανάλυση των LCO και LRO, υπολόγισε την 58η και την 52η επέμβαση ως σημείο αλλαγής, αντίστοιχα. Παρόλο που επιβεβαιώθηκε η παρουσία καμπύλης εκμάθησης στα παθολογοανατομικά καταληκτικά σημεία, αυτό δεν επετεύχθη για την μετατροπή σε ανοικτή επέμβαση και τις περιεγχειρητικές επιπλοκές.

Συμπεράσματα

Η καμπύλη εκμάθησης, απουσία ενός μεθοδικού προγράμματος εκπαίδευσης, επικυρώνει την συγκρισιμότητα των αποτελεσμάτων, ακόμα και στις αρχικές φάσεις της εκπαίδευσης. Ωστόσο τέτοιες πρωτοβουλίες είναι απαραίτητες για την ασφαλή και αποτελεσματική εφαρμογή των LCRO.

Abstract

Introduction

The present study displays our experience regarding the learning curve (LC) status of laparoscopic colorectal surgery, under a non-structured training setting.

Methods

A retrospective analysis of a prospectively collected database in our tertiary institute was performed. The surgical team consisted of two surgeons with no previous exposure to laparoscopic colorectal operations (LCRO). For malignancies, all the appropriate oncological principles were followed. All adult patients submitted to elective or semi-elective colon (LCO) or rectal surgery (LRO) were included. CUSUM analysis plots that confirmed a LC pattern, were further assessed through the change-point analysis (CPA).

Results

Overall, 133 LCOs and 81 LROs were performed. In terms of operative time, our LC in LCRO consisted of 3 phases. The CPA analysis identified the 110th case as the turning point of the first two phases. A plateau was reached after the 145th case. Subgroup analysis of the LCO and LRO, estimated the 58th and 52nd case as the turning points, respectively. Although we were able to confirm the presence of a LC pattern in the histopathological endpoints, this was not the case for the open conversion and morbidity outcomes.

Conclusions

The LC in the absence of a methodized training program validate the comparability of the results, even in the initial learning phases. However, such initiatives are necessary for the safe and efficient implementation of LCROs.

1. GENERAL PART

Colorectal Surgery

Colorectal operations are one of the most frequently performed procedures of abdominal surgery [1–3]. Although a multidisciplinary approach is, nowadays, applied, in both malignant and benign pathologies, ultimately, the majority of patients will undergo an operation [1–3]. More specifically, for colorectal cancer, it is estimated that 66% of cases will require at least one major resection [1–3].

However, in contrast to other abdominal operations, colorectal surgery displays a considerable morbidity and mortality profile. Current literature reports suggest that the mortality and morbidity rate of colorectal resections can reach the levels of 16.4% and 35%. Anastomotic leakage, a dreaded complication of GI surgery, is noted in 6.9% of cases [1–3]. In addition to these, reoperation rates in the various series, range between 2 and 5.8% [1–3]. The result of these, is a devastating effect in the survival, functional recovery and quality of life of the treated patients. Alongside, health care resources are greatly impacted [1–3].

Subsequently, quality improvement programs and audits (e.g. NSQIP, SCOAP, etc.) have been designed and implemented. Primarily these programs attempted to record the current trends in colorectal surgery and provide an exact estimation of the perioperative results. The next step included improving the results of all suboptimal endpoints [1, 3].

In order to enhance these outcomes, the quality of all components of the provided care should be individually assessed and optimized. The quality of the provided surgical care is based on the Donabedian model [3]. This theoretical model suggests that the overall quality is affected by three and interrelated components, structure (i.e. hospital and surgeon volume, nursing ratios, etc.), process (i.e. interventions, medications, etc.) and outcomes (i.e. morbidity, mortality, survival, quality of life, etc.) [3].

As a result, the protocols (ERAS, ERP) that have been introduced in colorectal surgery implement a holistic approach and address all potential risk factors of suboptimal postoperative performance [1, 3]. These protocols include early identification of frailty and sarcopenia, nutritional support, prehabilitation, early postoperative mobilization and feeding, reduced opioid-related analgesia and restricted fluid resuscitation and antibiotic chemoprophylaxis. A major component, though, is the minimization of the surgical trauma, through adoption of minimal invasive techniques.

The role of Minimal Invasive Abdominal Surgery

The introduction of the minimal invasive principles in abdominal surgery is considered as one of the most important breakthroughs of modern-day surgery [4–9]. The completion of standard procedures through small ports reduces postoperative pain, complications and enhances cosmesis. The smaller incisions, alongside the favorable pain profile and the lower analgesia requirements contribute to a shortened recovery period [4–9]. As a result, the benefits deriving from a minimal invasive approach in abdominal surgery have been displayed in both an acute and an elective setting.

A meta-analysis of RCTs by Cirocchi et al. [10] compared a minimal invasive approach versus the standard open laparotomy for perforated duodenal ulcers. Laparoscopy was associated with significantly lower postoperative pain scores and SSI risk. A benefit is also identified in elderly patients [5]. An interim analysis of the FRAILESEL study confirmed a safe profile of laparoscopic peptic ulcer treatment and suggested a lower blood loss volume and a shorter LOS. Interestingly the operation duration open surgery was longer.

A Cochrane meta-analysis by Jaschinski et al. [11] reported a lower rate of postoperative pain and SSIs for laparoscopic appendicectomy. Although minimal invasive appendicectomy increased the risk of intraabdominal abscesses, LOS and return to normal activities were significantly shortened. These were also confirmed in an umbrella review by Poprom et al. [4].

A large multicenter trial (LASSO), applying a laparoscopic approach in adhesive small bowel obstruction resulted to a decreased hospitalization period and a lower morbidity rate [8].

A recent meta-analysis [9] highlighted a multidimensional benefit from laparoscopy in small bowel obstruction, including reduced mortality, LOS, operative time, return of bowel function, morbidity and reoperation rate.

The superiority of laparoscopic abdominal surgery has been also documented in the elective oncological operations. A typical example is the LEOPARD trial [7], where a minimal invasive resection was associated with a significantly shorter functional recovery, blood loss volume and delayed gastric emptying complications. Similarly, the KLASS-01 trial [6] validated a lower rate of overall complications and SSIs.

Laparoscopy in Colorectal Surgery

Several RCTs and meta-analyses provided evidence regarding the comparison of open and laparoscopic colorectal cancer surgery.

In the JCOG0404 trial [12], the laparoscopic and open approach of colorectal surgery were assessed during the 3 investigating periods. In the rectal groups, only rectosigmoid tumors were included. The study confirmed a decrease in intraoperative blood loss during the latter periods. Although a gradual decrease in the complications rate of the open approach was noted, the laparoscopic group displayed a favorable morbidity profile. There was no difference between the two techniques in terms of 5 year OS or RFS [12].

The ACOSOG Z6051 [13] RCT compared the two modalities in terms of stage II/III rectal cancer. The initial report could not reach a statistical non inferiority threshold for the minimal invasive technique regarding pathological outcomes. Moreover, the two techniques were equivalent in recurrence rates and DFS. These significance of these results, though, was questioned due to an underpowered sample [13].

In the ALACART study [14], the researchers attempted to examine, whether the implementation of a minimally invasive technique in rectal cancer would have a negative impact on tumor clearance. The primary endpoint of this study was the non-inferiority of laparoscopic surgery in an adequate resection. The latter incorporated parameters such as a complete mesorectal excision and a clear CRM and DRM. Analysis of the accumulated data could not support the non-inferiority hypothesis [14].

In contrast to these the COREAN RCT [15] set the primary outcome of 3 years DFS, with a 15% non-inferiority margin. The sample size of the study consisted of mid and low rectal tumors after a neoadjuvant scheme. The conclusion of the trial was that the non-inferiority of laparoscopic rectal surgery was validated [15].

Moreover, the COLOR II study [16] confirmed that laparoscopic colorectal surgery was associated with longer operative duration, less blood loss volume, earlier return of bowel function and LOS. Pathological outcomes and morbidity and mortality rates were equivalent [16]. Analysis of the long-term follow-up outcomes confirmed a similar risk for bowel obstruction, incisional and parastomal hernia [17]. In addition to these, the DFS, OS and recurrence rated did not differ between laparoscopic and open colorectal approach [17]. These results were in concordance with the respective findings of the CLASSIC study, where survival and recurrence rates were comparable [18].

Based on these studies, subsequent meta-analyses attempted to confirm the safety and efficacy of the laparoscopic colorectal surgery. Liang et al. [19] could not confirm a superiority of the open approach in overall, local, distant or wound recurrence rates. Liu et al. [20] suggested a lower postoperative complication rate of laparoscopic colorectal surgery, with a similar pathological and survival outcomes. Finally, a recent meta-analysis by Wu et al. [21] attributed to the minimal invasive resections a pooled lower blood loss volume, faster bowel recovery, fewer adverse events and a shorter LOS. Intraoperative adverse events, mortality and leakage rates were similar to the open approach [21].

Besides malignancy, the advantages of the laparoscopic approach in colorectal surgery have been also displayed in benign pathologies, such as diverticular disease.

Senagore et al. [22], performed a cost structure comparison of laparoscopic and open sigmoidectomies for diverticular disease. In this study, all consecutive patients submitted to an elective resection for diverticular disease during the 1999-2000 period were included. Although the operative time was similar, LOS was significantly lower in the laparoscopic group. Pulmonary and wound complications were also less frequent when a minimal invasive approach was introduced. The open conversion rate was estimated to be 6.6%. Readmission and mortality rates were comparable. An interesting finding was that an open approach led to a significantly higher, overall, procedure cost [22].

Similar were the findings of Dwivedi et al. [23]. Blood loss volume, onset of liquid diet and LOS were significantly reduced when laparoscopy was applied in simple sigmoid diverticular disease. In contrast to the previous results, this study suggested that open sigmoidectomy was faster and the open conversion rate of laparoscopy was 19.7% [23].

In a prospective single blind RCT by Gervaz et al. [24], the longer operation duration of laparoscopic sigmoidectomy for diverticulitis was confirmed. It was also shown that postoperative pain and time to first bowel movement were significantly higher when laparotomy was applied. These resulted to an increased need for hospitalization, compared to laparoscopic surgery [24].

As a result, these advantages of laparoscopic colorectal surgery in benign pathologies were further validated in a recent meta-analysis by Cirocchi et al. [25]. In this review, laparoscopy was associated with a significantly lower rate of overall complications. However, an improved performance in LOS, primary anastomosis rate, operative time, reoperation rate and mortality was not confirmed [25].

Learning Curve

Due to the complexity of laparoscopic procedures, the notion of the learning curve has been introduced in the setting of minimal invasive surgery [26–28]. Learning curve is defined as the graphical representation of the learning effort and the respective learning outcome [27]. More specifically, the deliberate practice or the consecutive number of repetitive tasks is considered as the learning effort (x-axis), whereas the learning outcome is usually displayed in the form of measured performance (y-axis) [26–28]. The graphical representation of the learning curve is usually not linear and takes the form of an S-shape, thus suggesting that the learning rate is not steady throughout the learning period [26–28].

LCs have been extensively used in the industrial setting for the description of the output performance on the basis of the production quantity [27]. Correspondingly, LCs were incorporated in healthcare, upon the introduction of complex interventions, such as minimal invasive procedures [27]. Several LC evaluating studies have been published, thus highlighting the role of the learning status in aspects of medicine, such as RCT design, training program design and assessment of surgical performance [27].

The LC consists of 3 distinct phases. The initial phase of rapid learning is followed by a diminishing returns phase. Further proceeding in the LC results to an unlearning phase [26–28]. More specifically:

1st Phase of the Learning Curve

In the first phase of the LC, a rapid accumulation of skills and competence is achieved. Through deliberate practice and active feedback, the subject improves the results of assessed outcome, thus optimizing performance. The notion of a steep learning curve is widely applied in medical literature, suggesting difficulty in achieving competency in a specific task [26–28]. In fact, the graphical representation of a steep learning curve is synonym to acquiring a simple and not complicated skill [27].

A heterogeneity in the learning rates regarding a specific intervention among individuals is expected and justified. Factors that affect the slope of the initial LC phase include technological innovations, alterations in the guidelines algorithms, previous experience, formation of specialized teams and subject-related characteristics [27]. Among these individual characteristics are traits such as personal attitude, natural talent, motivation, and the ability to adopt and adapt to new skills [26–28].

2nd Phase of the Learning Curve

Once the initial phase of the LC has been completed, a 'plateau' is reached. It is considered, thus, that this phase is associated to mastering the studied intervention [27]. However, this does not necessarily translate to achieving expertise, but rather, a termination of the learning process [26–28]. Characteristically, in the graphical representation of the LC it is shown that the uptake of additional learning tasks does not lead to any improvement in the measured performance outcome. Therefore, in order to further increase the competency of an individual, alternative or additional learning strategies should be implemented [27].

In most studies, mastery is considered as the optimization of the evaluated endpoint. However, achieving competence includes the augmentation of several parameters, including technical, theoretical, cognitive, communicational and integrative skills [27]. The holistic, though, evaluation of LC is, still, not widely applied in current studies [27].

3rd Phase of the Learning Curve

A decline in the competency of the assessed individual can be seen once the performance of the repetitive tasks is resumed after the expert plateau [27]. This decline is subgrouped in two categories. The first one includes cases, where the subject displays a characteristic overconfidence in undertaking challenging tasks [27].The second etiology of this decline is the physiological process of ageing, where the evaluated individual displays a deterioration of the required cognitive and motor skills [26–28].

Learning Curve Analysis

The analysis of a learning curve can be performed in either an individual or group based level [26]. In the former, a linking equation is usually applied, whereas in the latter multivariable analyses attempt to identify confounders and perform group-based comparisons [26].

The characteristic of individual-based learning curve analysis, is the variance in the reported results [26]. This heterogeneity is the result of different starting levels and progression rates. Indeed, the morphology of a learner's curve allows the extraction of valuable information regarding the initiation, the progression and the stalling of the learning process [26]. An interesting finding in some individuals is that they may display a negative slope, especially, during the first phases of their curves. This is suggestive of an ineffective and malfunctioning learning process. Moreover, experienced individuals may also display flattened or even decreasing curves [26].

Group-based learning curve analysis allows the estimation of the average turning points of the learning process for a subgroup of individuals [26]. Since this method summarizes the results of several subjects, it provides a pooled evaluation of the learning curve [26]. This is specifically important for designers of educational programs, allowing the educator to adapt the training plan based on the estimated curve slopes. Furthermore, the use of regression techniques provides information regarding the parameters that, modified, will accelerate the skill transfer procedure. Finally, the pooled LC can be used as a benchmark upon which all future individual learners will compare their performance [26].

Variables

The validity of an LC is, primarily based on the use of proper and meaningful variables. Although it is suggested to use clinically significant indicators, many researchers base their analyses on the availability of data.

Several variables have been proposed for the x-axis of a learning curve [26–28]. Theoretically, the applied variable is a countable repetition or time measure that is directly related to the desired learning outcome [26–28]. It must be noted, though, that time is, generally, a low-quality variable for the x-axis, since it does not reflect the number of the repeated learning processes. The reasoning behind this is that the number of learning events over a unit of time may vary. Another factor that should be acknowledged prior to interpreting an LC is that the learning effect of each exposure in an intervention may vary due to different learning opportunities and heterogeneity in the complexity of case [26–28].

The variable that is applied in the y-axis of a LC graph is a representative measure of the learning process. Before selecting the appropriate variable for the learning curve analysis, researchers proceed in assessing the validity of their construct hypothesis [26]. Confirming the construct hypothesis is based on the identification of the following evidence: a) content evidence that consists of data displaying a test development behavior, b) relation evidence, where the association of data with other variables is displayed, c) response evidence, examines the fit between the construct and the performance, d) internal structure evidence that includes reliability, factor analysis and item analysis, and e) consequence evidence, where the intended or the unintended effects of the intervention are evaluated [26]. The two last types of evidence are specifically important, since they are frequently adopted as nominators of the learning process [26].

When evaluating an interventional learning curve, the y-axis can be a continuous (e.g. procedure duration, blood loss, LOS, etc.) or a dichotomous variable (success, reintervention, morbidity and mortality rates, survival outcomes, etc.) [26].

Two significant effects in LCs that may influence the estimated outcomes are the floor and the ceiling effect. These consist of a reduced variance of scores at the low and high end of performance scale, respectively [26]. These result to a vertically compressed learning curve [26].

Techniques for Evaluating the Learning Curve

A great variety of techniques have been used for the evaluation of the learning curve status [28]. The following are the most, commonly, used methods:

Descriptive

This technique does not include the performance of any statistical test. Instead, the data are tabulated over gradually increasing experience. Moreover, a graphical representation of the measured variable and the case sequence is plotted and inspected. The drawback of this technique is that results can be misleading in cases of data with increased variability [27, 28].

Split Group

In this approach, the evaluated data are divided in two or more consecutive chronological periods and compared on the basis of the assessed outcomes [27, 28]. The hypothesis in this method is to detect significant differences between the periods that would confirm the presence of a learning effect. The groups are compared through the application of univariate tests (t test, chi-square test, Mann-Whitney U test, ANOVA) [27, 28]. Since this approach is easy to use and does not require specialized statistical experience, it is widely used. However, the results of this analysis may be prone to bias and can be affected by several factors, including the arbitrary group size. Additionally, although a learning effect can be confirmed, the exact learning curve slope and turning points cannot be estimated [27, 28].

Univariate (trend)

In univariate trend analysis of the provided data, specialized statistical computations are performed in order to confirm the presence of a specific trend by experience. In some cases, the provided data may be spit in subgroups [27, 28]. The performed statistical analyses include chi-square test, repeated measures ANOVA, Spearman's correlation coefficient, Kolmogorov-Smirnov test and curve fitting analyses (e.g. least-squares regression, Monte Carlo simulation) [27, 28]. The curves that have been used for the description of the LC relationship between the two assessed two variables are the linear, the logarithmic, the negative exponential, the double negative exponential, the power form, the reciprocal, the quadratic and the cubic [27, 28].

It must be noted, though, that although high order functions may be fit a LC curve, they do not provide evidence regarding the learning rate or the plateau turning point [27, 28]. Moreover, fitting a function curve in a LC does not exclude the fact that another function may provide a better fit. As a result, novel studies suggested a mathematical algorithm of comparing the fit of the various proposed models [27, 28].

Multivariate (split)

In this approach the provided data are divided in groups based on experience and a multivariate testing is performed in order to adjust for other confounding variables. The statistical methodology includes logistic regression and Cox regression [27, 28].

Multivariate (trend)

In this method, the evaluated experience variable is adjusted for confounding variables. The applied statistical tests are logistic regression, multiple regression and generalized linear mixed models [27, 28].

Moving Average

A moving average function is frequently used for the determination of changes in measured data. Plotting a moving average over an evaluated variable allows the detection of changes on the rate of the experience accumulation. There are several types of moving averages, including simple, weighted and exponential. Special consideration should be made on the time interval that will be applied, since it alters the sensitivity of the moving average [27, 28].

CUSUM

The cumulative sum (CUSUM) technique is one of the most frequently applied techniques in assessing the presence of LC. It is a statistical method of detecting cumulative changes, thus confirming deviations from the expected course. The gradual accumulation of small changes results to the decrease of the data variance, thus highlighting a significant difference in the assessed individual's expected performance [27, 28].

The CUSUM plot displays the cumulative deviation from the expected performance. As a result the actual performance is estimated by the plot gradient for each specific timepoint [27, 28].

The CUSUM plot for continuous variables is calculated by the following equation [29]:

Sn=Σ(Xi-μ), where, as Xi is defined the value of each case and μ the mean

The CUSUM plot for categorical variables is calculated by the following equation:

Sn=Σ(Xi-X0), where Xi=0 for success and Xi=1 for failure and X0 is the reference of the target value.

The following is the standard CUSUM function [29]:

$$S_0 = 0$$
$$S_{n+1} = \max(0, S_n + x_n - \omega_n)$$

Moreover, the LC-CUSUM function is displayed below [29]:

$$S_t^1 = \min(0, S_{t-1}^1 + W_t^1), \quad S_0^1 = 0$$
$$S_t^2 = \max(0, S_{t-1}^2 + W_t^2), \quad S_0^2 = 0$$

where S^1 and S^2 are the test statisitics of the X_t observation and W are the rsepective weights. These are estimated based on the following equations for continuous and categorical functions, respectively:

$$W_t^1 = (X_t - \mu_0)/\sigma - g/2$$
$$W_t^2 = (X_t - \mu_0)/\sigma + g/2$$

where μ_0 the mean and σ the expected standard deviation.

$$W_t^1 = \log\left[\frac{p_0^{X_t}(1-p_0)^{1-X_t}}{(p_0+\delta)^{X_t}(1-p_0-\delta)^{1-X_t}}\right]$$

Where p_o the probability of failure when performance is adequate.

A risk adjusted LC-CUSUM can be also estimated, if the acceptable deviation is expressed in terms of odds ratio instead of an absolute risk difference. In that case, the following change should be considered [29]:

$$W_t^1 = \begin{cases} \log(1 - p_{0t} + \theta_\delta p_{0t}) & \text{if } X_t = 0 \quad \text{(success)} \\ \log(1 - p_{0t} + \theta_\delta p_{0t}) - \log\theta_\delta & \text{if } X_t = 1 \quad \text{(failure)} \end{cases}$$

Change Point Analysis

Change point analysis [30] is based on an iterative application of CUSUM charts and bootstrapping techniques that aim to identify changes in a consecutive series of data. This technique is based on the mean-shift model and assumes the presence of independent and identically distributed residuals. Bootstrap analysis allows the estimation of CIs and p values. The bootstrap techniques that can be used include the centile, bias-corrected, accelerated and jackknife methods [30].

Learning Curve Applications

Learning curve analysis has been extendedly applied in randomized controlled trials. In order to enlist in an RCT, the individual performing an intervention, should provide evidence of his competence and the relevant learning curve status. Although the retrieval of historical data for every participating individual can be a tedious and difficult to complete task, several large scaled RCTs consider specific skills and experience prerequisites [27]. In addition to this, during the analysis phase of an RCT, some researchers apply Bayesian Hierarchical models in order to adjust for the confounding factor of learning curve heterogeneity. However, this approach is associated with a reduced statistical significance, especially in cases of high data variability [27].

Education in health sciences applications have greatly benefited from the implementation of learning curves. LCs are considered as the optimal way of assessing an individual's learning status since they depict the relation of learning effort and gradual transition from incompetency to proficiency [26]. LC educational analysis provides both individual and group-based benefits. During an educational program, using LC will allow the coordinator to receive crucial information regarding the number of the required training repetitions, the presence of a latent phase and the turning point of the plateau phase. Moreover, it allows the direct comparison of the efficiency of different training methods. Furthermore, monitoring the various LCs allows the tutor to early identify and remedy any individual-based learning deficiencies [26].

Learning curves are a significant part of a self-learning process. In self-learning the individual undergoes a continuous cycle of learning, skill acquisition and constant appraisal of the competency status and learning efficacy. Based on this cycle, the individual, accordingly, adapts the learning strategy and methods [26]. Learning curve, through visual representation allow the individual to self-monitor the skills acquisition slope and reflect upon the learning process effectiveness. Additionally, the confirmation of a degrading LC phase, rationalizes the enrollment in a skills refreshing training program, in order to ensure the quality and safety of the provided care [26].

The effect of the various training protocols in shortening the required number of learning periods for a certain competency level can be characteristically depicted in a learning curve. Besides the design and monitoring of formal structured training programs, LCs enable the efficacy evaluation of novel techniques such as individual courses, labs and simulations. These latter allow the care provider to increase his exposure in the examined technique, thus enhancing skill acquisition, without compromising, though, the safety of the patients [27].

The staged transition from a incompetent novice to a reflective specialist with optimal efficacy and improving rate has been extensively described in the Dreyfus and Dreyfus model [26]. Ericsson et al., extended this model by suggesting the presence of a plateau upon which, only a purposeful training process allows further improvement [26]. The importance of these theoretical models has been acknowledged, and the monitoring of outcomes during the repetitive performance of a medical intervention has been widely accepted in daily practice. However, current medical education community question whether a time-based curriculum or competency-based curriculum should be applied in medical training [26]. In the former, student undergo a pre-specified training period and graduate with different competency levels [26]. However, in the latter, colleagues accumulate an equivalent amount of skills, but with different training time requirements [26].

Learning Curve Limitations

Despite these, LCs display several limitations, that should be acknowledged prior to the appraisal of their results. Overall, bias can be present in both the effort and performance assessment and the statistical technique applied. First, since LCs is based on the fit of daily practice data to a statistical model, a certain amount of bias should be expected. More specifically, the use of a non-fitting model will result to misleading results. Another bias introducing factor is the exclusion of significant effort-related factors from the structured model. Therefore, the effect of these factors in the learning process is not depicted in the statistical calculations. Typical examples include the motivation, rewards, emotional status and self-regulating and scheduling abilities [26].

A significant confounder that can be present during LC assessment is the synergy between the training technique and the applied effort. A typical example of this bias is fatigue and boredom which become more abundant during the task repetition. Finally, besides these, the presence of a floor or a ceiling effect may affect the estimated LC results [26].

Learning Curve in Medical Literature

Due to the wide acceptance of the learning curve in medical professions, the applied techniques and methodology have been extensively evaluated in the literature.

Ramsay et al. [28], performed a systematic review of the literature and attempted to identify all studies addressing the issue of the learning curve in health technology. Overall, the authors identified 272 trials that estimated a learning curve. Most studies applied a case series methodology (95%) in human subjects (96%). Only 2% of these studies were RCTs. The learning curves were applied for the evaluation of minimal invasive (51%), surgical (41%) or diagnostic interventions (8%). Individual operators and institution performance were assessed in 47% and 52% of cases, respectively. The majority of studies were performed in a tertiary center (36%). An intraoperative dichotomous variable was the most common primary endpoint (51%). Postoperative outcomes were analyzed in almost 28% of studies. The most frequently applied statistical techniques were group splitting (60%), descriptive statistics (44%) and univariate trend analysis (12%). CUSUM charts were implemented in only 2% of cases [28].

Maruthappu et al. [31], screened the medical literature about studies reporting on the learning curve of surgical interventions and evaluated their methodology. Overall, 101 studies and 14455 assessed surgeons were introduced in this review. Although a gradual increase of the publishing rate of studies reporting on LCs was noted, only a small percentage of them applied a prospective (33.7%) multicenter (23.8%) design. Statistical modelling was applied in 41.6%. Adjustment for case mix (39.6%) and for surgeon specific factors (16.8%) were employed at a low rate. Regarding the analyzed outcomes, the most common were operation duration (59.4%), morbidity (45.5%), reoperation (29.7%) and mortality (15.8%). Learning curve graphs were provided in only 48.5% of studies. Based on these, the researchers proposed a framework for future studies monitoring surgical performance [31].

Another review [32], focused on the LCs of minimal invasive abdominal surgery. In this study, 592 analyses were identified. Similar to previous reports, the majority of the eligible studies were case series (93%) that involved laparoscopic general surgery operations (46%). The assessed operator was either an attending surgeon (87%) or a trainee (38%). An interesting finding was that in 17% of the studies the performance in simulation or animal models was evaluated. Performance assessment was based on operation duration (86%), intraoperative (53%) or postoperative outcomes (52%) and technical skills (17%) [32].

In a subsequent study, Barrie et al. [33], limited their analysis in LCs of laparoscopic or robotic assisted colorectal surgery. The researchers identified 28 laparoscopic and 6 robotic assisted trials. In contrast to previous results, CUSUM analysis was used in 47% of studies. Evaluation of LC patterns in multiple endpoints was applied in a significant proportion of the eligible sample (26.4%). A remarkable heterogeneity in the definition and estimation of proficiency was noted, with the latter ranging from 5 to 310 cases and 15 to 30 cases for laparoscopic and robotic operations, respectively [33].

Learning Curve in Open Colorectal Surgery

Despite including multiple intraoperative and sequential steps, open colorectal surgery is, generally, considered as less complex compared to the respective minimal invasive approaches, thus rendering it ideal for the initial phases of surgical training [34]. However, the effect of specialization, case volume and adequate mentoring on the perioperative outcomes has been documented [35].

In a retrospective analysis by Maeda et al. [36], 32 open colorectal resections were submitted to CUSUM analysis. The authors reported that operative time decreased with the accumulation of surgical experience and reached a plateau after the 22nd case. The respective learning curve was estimated at 11 operations [36].

Georgiou et al. [37], assessed the number of cases required for obtaining competency in advanced rectal tumors. Adjusted regression analysis showed that morbidity was affected by the application of neoadjuvant therapy, with no effect, though, of surgical experience. Risk adjusted CUSUM calculations confirmed that, regarding overall adverse events, the learning point was at the 14th case. For major and minor complications, the respective turning points were 12th and the 25th case. Positive margin analysis could not confirm the presence of an LC pattern [37].

Tekkis et al. [38], in a series of 1965 cases evaluated the role of training in the postoperative results of the IPAA anastomosis. A LC pattern was confirmed in 50% of the surgeons. For stapled anastomosis, the training point was estimated at 23 and 40 cases for junior and senior surgeons, respectively. Hand-sewn anastomosis, though, displayed a longer training period (31 operations) [38].

Learning Curve in Laparoscopic Colorectal Surgery

The pattern and the length of the laparoscopic colorectal surgery learning curve has been a topic of significant research effort in the last decade. Bennett et al. [39], analyzed 1194 patients operated by 114 surgeons that were included in a prospective registry. Surgeons were categorized as either high (more than 40 cases) or low volume (less than 40 cases). In this study, laparoscopic assisted resection of the small bowel, colon or rectum (91.2%), intestinal bypass (4.1%) and polypectomy (0.9%) was included. Anastomoses were more frequently performed in an extracorporeal fashion (59.6%). The most common pathology was malignancy (42.2%), polyps (19%) and inflammation (24.3%). The researchers reported that the laparoscopic completion of the operation and the LOS was not affected by the volume of the operating surgeon. Instead, complications rate was significantly lower in high volume surgeons

(10% vs 19% P<0.001). In adjusted regression analysis, it was shown that high volume surgeons displayed an optimal profile in terms of both intraoperative (OR: 0.56, P=0.04) and postoperative adverse events (OR:0.48, P<0.001) [39].

Prakash et al. [40], in a retrospective analysis from a single center, compared the outcomes of the initial 132 cases with the next 133 laparoscopic colorectal operations. The latter group was associated with a higher rate of comorbidities (63.2% vs 32.5%) and low rectal lesions (33.8% vs 20.4%). The accumulation of experience affected operative time and blood loss, but not conversion rates. Additionally, in the second group a shorter duration of ICU admission, LOS and NGT stay was identified. Finally, it was reported that experienced surgeons tended to operated a higher rate of locally advanced tumors [40].

In a similar trial by Chen et al. [41], 100 laparoscopic colectomies were divided in two groups of 50 cases, based on a consecutive order. Preliminary analysis showed that the two groups were comparable in terms of demographics and tumor stage. The investigators suggested that, in terms of operative time, a plateau was reached after the 23rd patient. However, they could not confirm any difference in the other perioperative and pathological outcomes [41].

Selim et al. [42] applied both the moving average and CUSUM analysis for the estimation of the LC in laparoscopic sigmoidectomies of two self-educated surgeons. Regarding operation duration, LC turning point ranged from 90 to 110 cases. Respectively, in terms of open conversion and morbidity, a plateau was reached after the 70th-80th case [42].

Li et al. [43], analyzed all consecutive patients submitted to laparoscopic colorectal surgery during the 1992-2008 period. The learning curves of the institution and of each individual surgeon were estimated by using the CUSUM approach. Overall, 1031 operations were performed. CUSUM analysis confirmed that the conversion rate stabilized after the 310th

case. Moreover, intraoperative and postoperative complications reached a plateau after the 50^{th} case [43].

Son et al. [44], used multiple statistical techniques, including CUSUM, risk adjusted CUSUM and ANOVA analyses in order to analyze the LC of laparoscopic rectal operations. Prior abdominal surgery and tumor size>3 cm were considered as risk factors for open conversion. The estimated LC turning point for the open conversion was the 61^{st} case. Considering postoperative morbidity, the 79^{th} case was found to be the LC peak. Respectively, LC analysis for the operative time and the transfusion volume identified the presence of a plateau during the 61^{st}- 75^{th} case [44].

Some researchers attempted to compare the learning curve of laparoscopic colorectal operations, based on the resection side. Tekkis et al. [45], performed a single center retrospective study that included 900 patients from the Cleveland Clinic. The analysis of these data was based on a multifactorial logistic regression analysis and a subsequent risk-adjusted CUSUM model. The researchers reported that the conversion rate for the right and left-sided resections was 8.1% and 15.3%, respectively. Analysis identified several open conversion predictors, including BMI, ASA, type of resection, presence of abscess or fistula and surgeon's experience. The completion of the adjusted CUSUM analysis showed that the learning curve turning point for the right and left sided operations was 55 and 62 cases, correspondingly. An interesting finding was that, although, readmission and morbidity rates were unaffected, operative time decreased throughout the LC [45].

In a single-surgeon retrospective analysis by Park et al. [46], a CUSUM technique was applied for the estimation of the LC. Initially, 1014 cases were divided into nine consecutive periods (1^{st}: 1-30 cases, 2^{nd}: 31-58 cases, 3^{rd}: 59-100 cases, 4^{th} to 7^{th} period each 100 cases, 8^{th}: 501-800 cases, 9^{th}: 800-1014 cases). The authors reported that a gradual decrease of operative time for right hemicolectomy and anterior resection was noted. However, operation duration of low anterior resection displayed a plateau until the 9^{th} period, where a significant decrease was estimated. Lymph-node yield in right colectomies stabilized to 35-40 nodes after 200 cases. However, in rectal surgeries, the node yield was systematically 15-20 nodes after the first 20 cases. Open conversion CUSUM analysis suggested the 13^{th} case as the point of the target success rate [46].

In a systematic review by Miskovic et al. [47], 23 studies were identified that evaluated the LC in laparoscopic colorectal surgery, with a notable diversity in the reported outcomes. Pooled risk adjusted CUSUM analysis estimated the following turning points of the various outcomes: 152 for open conversion, 143 for morbidity, 96 for operation duration, 87 for blood loss and 103 for LOS. Based on their risk analysis, the authors, also, proposed the optimal case complexity characteristics for each LC status. The risk predictors included the BMI, the resection type, the T stage and the inflammatory complications [47].

Colorectal Surgery Training

As an answer to the long learning curve of laparoscopic colorectal operations, several structured training programs have been introduced [48, 49]. These programs include an initial phase where the surgeon acquires the necessary psychomotor skills in a non-clinical setting, including wet labs, lectures and courses [48, 49]. Once this is achieved, the surgeon performs the first operations under the guidance of a mentor [48, 49]. As a result, the surgeon ascends the LC in a safe and efficient setting [48, 49].

The association between formal training in colorectal surgical training and the LC was evaluated by several researchers. Choi et al. estimated the LCs of 3 surgeons who had completed a colorectal surgery fellowship program and had previous laparoscopic experience [50]. Moving average analysis of the operation duration showed that the plateau was reached after the 30^{th}-42^{nd} case. CUSUM analysis, though, suggested that adequacy was achieved after the 5^{th}-17^{th} case [50].

In a study by Li et al. [51], the LC of a colorectal fellow that underwent a structured training program was assessed. This program included assisting in more than 40 cases before performing the first laparoscopic colectomy. Analysis of the results showed that operation duration reached a nadir during the 45^{th}-50^{th} case. Another interesting feature of this study was that the fellow required more frequently the presence of a supervisor in the theater during the first 50 cases (74% vs 52%). The comparability of the clinical outcomes between the two periods, further confirmed the safety of performing laparoscopic colorectal operations in a fellow setting [51].

Another study by Nijhof et al. [52] attempted to confirm the safety of performing laparoscopic colorectal surgeries during training. The authors compared the postoperative outcomes of a supervised fifth- or sixth-year resident and a dedicated colorectal surgeon. Although the former was associated with a higher conversion rate (3.57% vs 8.26%), operative time, blood loss, morbidity and oncological outcomes were comparable [52].

Similarly, Kye et al. [53], reported that laparoscopic right colectomies performed by an experienced and adequately trained colorectal surgeon reached earlier the peak lymph node yield (37^{th} vs 8^{th} case). Further CUSUM analysis in terms of intraoperative failure showed that the LC of the trained surgeon required less cases (18 vs 8) [53].

Besides these, training and adequate experience of both the operating surgeon and the assistant is necessary for optimal results in laparoscopic colorectal surgery. In a retrospective study, Hwang et al. [54], applied the moving average method to assess the assisting competency of surgical fellows. Thus, it was reported that, 30-40 cases are required for an assistant to optimize the execution time and the error rate for tissue grasping [54].

Specialized Colorectal Surgical Teams

Moreover, the role of the specialized colorectal teams has been extensively assessed for their role in enhancing the postoperative outcomes. In a recent study, colorectal surgeons were compared with junior, not specialized, colleagues on the basis of oncological outcomes and postoperative recovery [55]. It was confirmed that operations performed by senior surgeons displayed a higher lymph node yield, a lower operative duration and lower blood loss volumes. Additionally, a significantly lower open conversion rate was identified in the senior group (20.7% vs 10%). Finally, regarding rectal tumors, experienced surgeons performed more frequently sphincter preserving operations (68.7% vs 35.3%) [55].

Li et al. [43], divided 1031 consecutive laparoscopic colorectal operations that were performed in their institution in two periods. In the first period the operations were performed by a general surgical team, whereas in the latter period, a sub-specialized colorectal surgical team was introduced. The authors reported improvements during the second period, in terms of operative time, lymph node yield, intraoperative blood loss and transfusion rates. Moreover, the specialized surgical group was associated with a significantly lower conversion rate (19.7% vs 5.1%) [43].

Besides LC, the role of specialized colorectal teams has been, also, evaluated in postoperative outcomes. Jeganathan et al. [56], analyzed 56216 colon and 10462 rectal resections from a large national database. The authors confirmed that operations performed by specialized surgeons and further by board certified colorectal surgeons increased the rates of adequate lymphadenectomy [56].

Similarly, Hall et al. [57], validated an association between colorectal specialization and survival outcomes. The authors included 27325 colorectal operations in their study. They reported a significant effect of specialization in disease free survival of stage II rectal cancer [57].

Objectives

Based on these evidence, we designed and implemented the present study, in order to report our experience regarding the learning curve status of laparoscopic colorectal surgery, under a non-structured training program.

2. SPECIFIC PART

Introduction

The implementation of minimal invasive principles in colorectal surgery has been a major achievement during the last two decades [58]. Several trials and meta-analyses highlighted the enhanced perioperative outcomes of the laparoscopic approach, such as reduced postoperative pain, morbidity and overall length of hospitalization [59].

However, these benefits come to the cost of a notably steep learning process [44, 60, 61]. The complexity of these operations, alongside the innate dexterity prerequisites of a minimally invasive approach, render training in laparoscopic colorectal skills challenging [37, 62–64]. Therefore, similarly to other multistep invasive processes, the assessment of a surgeon competency through a learning curve was universally adopted [65–68].

Although a remarkable heterogeneity in the learning curve turning points of laparoscopic colorectal surgery is identified in the literature, it is widely accepted that a minimum number of about 100 cases is required for achieving a decent proficiency level [40, 45, 69, 70]. During this period of experience accumulation, a parallel fluctuation in perioperative outcomes, such as complications and conversion to open surgery is noted [41, 42, 44, 47, 54, 71–73].

Consequently, for establishing patient's safety and promoting surgeons' training, an attempt was made to identify risk factors of the learning curve prolongation [40, 47, 74]. As an answer, the development of structured nation-wide training programs in laparoscopic colorectal surgery resulted in the easier surpassing of the learning curve [75–77]. Key characteristics of these programs include the establishment of dedicated surgical teams, the promotion of specialized training courses including mentorship and proctorship and the step-by-step optimization of the intraoperative tasks [53, 75–77]. However, these programs are not universally available, thus prohibiting the efficacious implementation of laparoscopic colorectal surgery [41, 62, 78].

Therefore, we designed this study, in order to analyze our experience regarding the learning curve of laparoscopic colorectal surgery, outside a formal national or surgical society driven training program.

Materials and methods

Study Design

This study is a retrospective analysis of a prospectively collected database. During the 2012-2019 period, data from all laparoscopic colorectal operations performed by a specialized surgical colorectal team have been recorded in our institutional database. All patients provided an informed consent prior to their inclusion.

The surgical team consisted of two specialized, board-certified, colorectal surgeons with experience in laparoscopic surgery. None of them had previous exposure to minimal invasive colorectal operations. During the study period the surgeons attained specialized courses and performed the initial operations under expert guidance, without registering in any structured training program for laparoscopic colorectal surgery. The team, also, encompassed a single dedicated pathologist responsible for examining the resected specimens. Feedback among the team members was essential.

Interventions

All operations were performed using 3-5 trocars in a standardized fashion. Dissection was performed using an energy source. A medial to lateral approach was implemented in all cases. For cancer surgery the appropriate oncological principles were followed [79, 80]. Identification and adherence to the proper embryonical plane (CME/TME) alongside CVL was performed in every malignancy case. In addition, a structured pathology report was applied [80, 81].

Considering laparoscopic right hemicolectomy, the patient was positioned in a modified lithotomy position, with the legs placed on stirrups [82]. The left arm of the patient was tucked on the trunk. The abdomen cavity was accessed through an open Hasson technique, thus allowing the placement of 10-12mm port sub-umbilically. Pneumoperitoneum was set at 12mmHg. Under direct vision, the following trocars were placed: 12mm in the left lower quadrant, 5 mm in the epigastrium and an auxiliary in the right abdomen. Once proper pneumoperitoneum was installed and all trocars were placed, a diagnostic laparoscopy was performed [82]. Following this, the right side of the patient was tilted up. A Trendelenburg or an anti-Trendelenburg position was applied based on the procedure phase. The omentum alongside the transverse colon was, then, retracted in the upper abdomen. After proper retraction of the cecum and identification of the ileocolic vessels, a dorsal and parallel to the ileocolic vessels, incision of the peritoneum was performed [82]. In continuum, a blunt dissection of the Toldt's fascia towards the lateral abdominal wall was applied. The dissection was continued until above the duodenum and until the junction of SMV and gastrocolic trunk [82]. The ileocolic vessels were, then, dissected and divided with an energy source or a laparoscopic stapler / clip applier [82]. The next step included the identification of the right branch of the middle colic artery. Following this, the lateral peritoneal reflection of the right colon, along the white line of Toldt was dissected. A medial to lateral division of the omental attachments at the transverse colon was performed, and the lesser sac was entered. This allowed the mobilization of the hepatic flexure [82]. An intracorporeal division and clipping of the right colic artery and the right branch of the middle colic artery was performed [82]. Subsequently, the mesocolon along the resection line was divided by using the energy source [82]. Similarly the mesentery of the terminal ileum was divided. Both the terminal ileum and the transverse colon were transected using a linear stapler. Anastomosis was performed either intra or extracorporeally, using a stapler or handsewn, based on the preferences of the surgeon [82]. A umbilical or Pfannestiel laparotomy was, then, performed for the extraction of the specimen. A wound protector was, always, applied, before the extraction of the specimen [82]. After laparoscopic inspection and proper hemostasis the ports were removed under direct vision. Drains were placed on the basis of the surgeons' preferences. The extraction site was closed, and the remaining port sites were clipped.

A similar approach was used for left colectomies and sigmoidectomies [82]. The patient was positioned in a modified lithotomy position, with the legs placed on stirrups [82]. The right arm of the patient was tucked on the trunk. The operating surgeon and the first assistant stand on the patient's right side. The abdomen cavity was accessed through an open Hasson technique, thus allowing the placement of 10-12mm port sub-umbilically. Pneumoperitoneum was set at 12mmHg. Under direct vision, the following trocars were placed: 12mm in the right lower quadrant, 5mm in the epigastrium and an auxiliary 5mm in left abdomen. The patient was tilted left side up and in a Trendelenburg position. Once proper pneumoperitoneum was installed and all trocars were placed, a diagnostic laparoscopy was performed [82]. The origin of the IMA and the superior rectal artery was, then, identified [82]. An incision of the retrorectal fascia at the level of the promotory was performed. A sharp dissection of the TME plane, ventral of the presacral nerves was completed [82]. The peritoneal fascia was incised towards the level of the sigmoidal and the IMA arteries [82]. Subsequently, a blunt dissection of the posterior plane of the left colon was performed in a medial to lateral fashion. The IMA or the sigmoidal arteries were divided using an energy source or aa stapler [82]. Following this, the IMV was identified and divided. The lateral peritoneal reflection of the left and sigmoid colon was dissected along the Toldt line [82]. Based on the pathology and the available resection margins, the transection sites were chosen. The mobilization of the splenic flexure included the following steps: dissection of the posterior aspect of the left colon cranially to the level of the spleen, identification of the pancreas, entrance to the lesser sac and division of the splenocolic and phrenicocolic ligaments. This approach allowed a tension free anastomosis. The mesocolon and the mesorectum were then divided using the energy source. An endostapler was used for the division of the bowel. A umbilical or Pfannestiel laparotomy was, then, performed for the extraction of the specimen. A wound protector was always applied in the extraction site. Anastomosis was performed either intra or extracorporeally, using a stapler or handsewn, based on the preferences of the surgeon [82]. Anastomotic air test was used for the confirmation of a properly sealed anastomosis. Protective stoma was based on the preferences of the surgeon [82]. After laparoscopic inspection and proper hemostasis the ports were removed under direct vision. Drains were placed on the basis of the surgeons' preferences. The extraction site was closed, and the remaining port sites were clipped [82].

In case of rectal pathology, the principles of TME was applied [83]. The application of the TME involves the sharp pelvic dissection and the preservation of the fascia propria of the rectum. The rectum, alongside its blood supply and the draining lymph-nodes is contained within this tissue envelope. Laparoscopic total mesorectal excision was completed by using monopolar hook diathermy or a laparoscopic energy source. The rectum was considered as a 4-sided box containing an anterior, posterior, left and right lateral side [83]. The initial phase of the TME began with the posterior dissection, above the pre-sacral fascia, that extended up to the pelvic floor [83]. Care was taken to avoid injuring the pre-sacral vessels. After the completion of the posterior dissection, the lateral mobilization was performed. The initial incision was performed 2cm above the peritoneal reflection. The lateral dissection is, then, continued anteriorly. The exposure of the proper embryonal plane was secured by proper traction and counter traction. Care was taken to avoid injury to the lateral pelvic nerves, since their proximity to the dissection plane, placed them at risk for mechanical or thermal injury. Based on the site of the pathology and the available resection margins the completion of an anterior or an abdominoperineal resection was considered. In the first case the rectum was divided using a stapler [83]. Anastomosis was completed through the application of a circular stapling device in an intracorporeal or extracorporeal fashion [83]. Following the leak test, the abdomen was irrigated, a drain was placed and the laparotomy was closed. A defunctioning ileostomy was completed based on the preferences of the surgeon [83].

In case of an abdominoperineal resection, the anus was sutured and closed with purse-string sutures [84]. An end colostomy was previously performed and the abdominal cavity was closed [84]. The patient was placed in a modified Lloyd-Davies or a jack-knife position [84]. The anatomical landmarks were identified (coccyx, bilateral ischial tuberosity, perineal body). After a skin incision, the subcutaneous fat is excised [84]. The sphincteric complex was included in the resection and the peritoneal cavity was entered after the anococcygeal ligament was incised [84]. The specimen was freed circumferentially and passed through the perineal incision. Once the specimen was extracted, the pelvic incision was closed in layers and a closed drain was placed [84].

Eligibility Criteria

As eligible were considered all adult patients (age>18 years) that were submitted to elective or semi-elective laparoscopic colorectal surgery for benign or malignant pathology. The exclusion criteria of our study were the following: 1) age< 18 years, 2) ASA>III, 3) emergency surgery, i.e. peritonitis, perforation, 4) cases not performed by the above-mentioned group.

ASA score was defined as following:

- ASA I. A normal healthy patient
- ASA II. A patient with mild systemic disease
- ASA III. A patient with severe systemic disease
- ASA IV. A patient with severe systemic disease that is a constant threat to life

- ASA V. A moribund patient who is not expected to survive without the operation
- ASA VI. A declared brain-dead patient whose organs are being removed for donor purposes

Endpoints

The primary endpoint of our study was to identify the learning curve status of the operation duration in patients who were submitted to laparoscopic colorectal operations (LCRO), colon operations (LCO) or rectal operations (LRO). Operation duration was measured from first incision to skin closure. Secondary analyses were performed on other operative characteristics indicative of surgeon's performance, such as overall complication and open conversion rate, resected specimen length and lymph node yield. Complications assessed were any Clavien-Dindo ≥2 adverse event.

Conversion was defined as, either the inability to complete the operation laparoscopically, or the extension of the mini laparotomy for any other reason except specimen extraction.

The Clavien-Dindo classification [85] of the postoperative adverse events was defined as following:

- Grade I. Any deviation from the normal postoperative course without the need for pharmacological treatment or surgical, endoscopic, or radiological interventions
- Grade II. Requiring pharmacological treatment with drugs other than such allowed for GI complications. Blood transfusions and total parenteral nutrition are, also, included.
- Grade III. Requiring surgical, endoscopic, or radiological intervention.
    - a. Intervention not under general anesthesia.

- b. Intervention under general anesthesia

- Grade IV. Life threatening complication (including central nervous system complications) requiring intermediate/intensive care unit management.
  - a. Single organ dysfunction
  - b. Multiple organ dysfunction
- Grade V. Patient death

Data Collection

The collected data included information regarding the demographic (gender, age, BMI, ASA and previous operation), disease (benign, malignancy and the respective stage) and operation characteristics (emergency status, duration, laparoscopic approach, extraction site and anastomotic technique) of each patient. Postoperative outcomes, such as operation duration, open conversion, transfusion, morbidity and mortality rate and length of hospital stay (LOS) were, also, recorded. Finally, pathology characteristics (tumor diameter, specimen length, distal margin, lymph node yield and ratio, grade, R status, vascular and perineural invasion and presence of mucous) of the resected tumor specimens were provided.

Statistical Analysis

Prior to any statistical analysis, a Shapiro-Wilk normality test was applied to all continuous variables [86]. Since normality was not proven, a non-parametric approach was implemented. Mann-Whitney U test was used for the comparison of continuous variables. Kruskal Wallis H test was applied for the analysis of multiple continuous variables. Pearson chi square test was implemented in the categorical variables. Z test was introduced for the comparison of proportions. Influencing factors were assessed through a Spearman's Rank-Order correlation test.

In order to identify variations in the changing rate of the studied variables and plot the respective learning curve (LC), cumulative sum (CUSUM) analysis was performed [87, 88]. CUSUM analysis was applied to all the above-mentioned endpoints.

The CUSUM analysis plots that confirmed a significant LC pattern, were further assessed and the existence of curve turning points was examined through the change-point analysis (CPA) [89]. CPA allows the identification of even small trend shifts and provides the respective statistical significance of each change. The CPA analysis was performed through the application of 1000 bootstraps, and a 50% CL for candidate changes.

Continuous data were reported in the form of Median (Interquartile Range), whereas categorical variables were provided as N (Percentage). Significance was considered at the level of $P<0.05$. Statistical analyses were completed through the use of STATA v.13 and SPSS v.23 software.

Results

The characteristics of the included patients are summarized in Table 1. In total, 214 LCRO (133 LCO and 81 LRO) were introduced in our study. The two study groups were comparable in terms of age (71 vs 68 years), BMI (28 vs 26.5 kg/m^2) and gender allocation (58.6% vs 61.7% males). A higher ASA II/ ASA I rate was noted in LCO (59.4% / 26.3%), when compared to LRO (46.9% / 44.4%).

In LCO, the diagnoses rates were the following: 94% malignancy, 4.5% diverticulitis, 0.8% volvulus and 0.8% Crohn's disease. In LRO, all cases (100%) included a malignant pathology. Regarding tumor classification, 33 T1, 39 T2, 47 T3 and 6 T4 tumors were included in LCO. Moreover, 89 and 30 cases were N0 and N1 respectively. In LCO, no patient was M1. Correspondingly, in LRO, the T grades were the following: 18 T1, 24 T2, 38 T3 and 1 T4. Furthermore, 64 N0 and 12 N1 cases were included. Only one case (1.3%) was metastatic in LRO. Only two patients in LCO had received neoadjuvant modality, compared to 17 in LRO.

Thirteen (9.8%) patients in LCO group and four (4.9%) in LRO, had previous abdominal operations.

Overall, 76 (35.5%) right colectomies, 31 (14.5%) left colectomies, 26 (12.2%) sigmoidectomies, 72 (33.6%) LAR, 7 (3.3%) ULAR, and 2(2.4%) APRs were performed. Regarding the emergency status of the operations, 212 (99.1%) and 2 (0.9%) cases were elective and semi-elective, respectively. 85% of the LCRO were performed in a totally laparoscopic manner, whereas in 15% of the cases a laparoscopically assisted approach was applied. Bowel preparation was administered to more LRO (97.5%), compared to LCO (84.2%). Regarding further preoperative optimization in terms of antibiotic bowel preparation (95.5% vs 97.5%) and tattooing (21.1% vs 28.4%), the two study groups were similar.

The majority of the anastomoses (75%) were performed using a stapler. More handsewn anastomoses were performed in the LCO compared to LRO (39.8% vs 0%). A higher rate of intracorporeal anastomoses (78.4% vs 37.6%) was documented in LRO. A significant difference in the intracorporeal/extracorporeal anastomosis ratio of the two groups was confirmed (37.6%/62.4% vs 78.4%/21.5%). A significantly higher rate of protective stomas was performed in LRO (70.4% vs 6.8%).

A higher median operative time was identified in LRO group (200 vs 180 min). Moreover, a higher open conversion rate (17.3% vs 4.5%) was documented in LRO. Transfusion rates between the two groups were comparable (3% vs 4.9%).

The overall complication rate was estimated at the level of 22.9%, with no difference between LCO and LRO (24.8% vs 19.8%). The estimated pooled rate of the various adverse events was the following: 4.2% wound infection, 0.9% wound dehiscence, 6.5% leak, 5.1% postoperative ileus, 0.9% urinary tract infection, 0.9% urinary retention, 1.4% bleeding, 0.9% pulmonary embolism and 0.5% ARDS. In addition to these, the rates of relaparotomy (6% vs 3.7%), ICU admission (3.8% vs 3.7%) and mortality (3% vs 1.2%) were comparable among the two subgroups. A comparable LOS (2 vs 2 days) was, also, reported. The duration of postoperative follow-up in the two groups did not differ (2 vs 2 months).

Table 1, also, summarizes the histopathological characteristics of the specimens. Tumor diameter was similar between the two groups (3 vs 3.75 cm). A significantly higher specimen length was reported in the LCO group (21 vs 15 cm). R0 resection was achieved in 95.3% of the patients. The majority of the tumors (65.5%) were moderately differentiated. The median resection distal margin was 5.25 cm and 4.55 cm for LCO and LRO, respectively. The lymph node yield in the LCO and LRO groups was 19 and 15 nodes, respectively. A comparable positive LN ratio was validated. The rates of extramural vascular invasion (26.4% vs 25.9%) and perineural invasion (10.4 % vs 9.9%) was similar between LCO and LRO. A focal or diffuse mucous component was found in 29 (14.1%) and 20 (9.7%) cases, correspondingly.

In Table 2, a summary of the results of the Spearman's Rank Order correlation test regarding the operation duration were reported. Regarding the overall operation duration, a significant association with the following variables was identified: sex (P=0.002), diagnosis (P=0.01), distance from the anal verge (P<0.001), operation type (P=0.001), laparoscopic approach (P<0.001), administration of neoadjuvant scheme (P<0.001), tattooing (P=0.023), extraction site (P=0.005), anastomotic technique (intra/extracorporeal P=0.048, stapled/handsewn P=0.04), completion of a protective stoma (P<0.001) and tumor diameter (P=0.014). In LCO, a higher operative time was related with the male gender (Spearman's P= 0.015), the diagnosis of malignancy (P= 0.04), a laparoscopically assisted approach (P= 0.001), the administration of neoadjuvant modality (P= 0.02), a higher tumor diameter (P= 0.006) and specimen length (P= 0.001). Similarly, in LRO, a longer operation duration was correlated to the male gender (P= 0.015), a laparoscopically assisted approach (P= 0.005), a neoadjuvant scheme (P= 0.006), the lack of preoperative tattooing of a lesion (P= 0.001), and the formation of a protective stoma (P <0.001).

Regarding CUSUM analysis, the LC considering the operation duration of laparoscopic LCRO is displayed in Figure 1. Inspection of the chart, reveals a significant decrease of the CUSUM line, up to the 109th case, where it reaches its minimum value and a consequent increase, until it peaks at the 176th case. CPA analysis (Figure 2), identified a significant turning point of the LC at the 110th (CL: 100%) and 145th (CL: 99%) case. Based on these results (Table 3), we identified three phases of the laparoscopic colorectal operations learning curve (Phase I: 1-109 cases, Phase II 110-144 cases and Phase III: 145-214 cases).

CUSUM LCs for LCO and LRO are provided in Figure 3 and 5, respectively. A similar pattern was identified in both plots. LC was characterized by an initial steady decline until a minimum turning point and a subsequent increment of the CUSUM plot value. More specifically the 58th (CL: 99%) and the 52nd (100%) were estimated as the CPA analysis (Figure 4 and 6) turning points for LCO and LRO, respectively. Therefore, the LC in LCO and LRO was divided in two phases (LCO Phase I: 1-57 cases, Phase II: 58-133 cases and LRO Phase I: 1-51 cases, Phase II: 52-81 cases).

In Table 3, the allocation of the patient characteristics and the perioperative endpoints between the different LC phases is displayed. In LCRO, a lower percentage of the operations were performed totally laparoscopic in Phase II (68.6% vs 89.7% in Phase I and 85.7% in Phase III). A gradual decrease in the rate of the patients receiving bowel preparation was noted during the three LCRO phases (Phase I: 98.2%, Phase II: 85.7% and Phase III: 77.1%). Moreover, LCRO Phase III was characterized by a significant improvement in the specimen length ($P<0.001$), the resection distal margin ($P<0.001$) and the lymph node yield ($P=0.016$). A higher rate of foci mucous was identified in Phase II (54.5% $P=0.006$).

Subgroup analysis of these results showed that in the LCO Phase I a higher percentage of patients had undergone previous operations (15.8% vs 5.3%, $P=0.04$). Moreover, less patients received bowel preparation (98.2% vs 73.7% $P<0.001$) and tattooing (29.8% vs 14.5%

P=0.032) in LCO Phase II. Furthermore, experience in LCO resulted in a longer distal resection margin (p<0.001) and a higher lymph node yield (p=0.002). A higher rate of Grade II tumors was identified in LCO Phase II (80.5% vs 58.5% P=0.009). More patients received a neoadjuvant scheme in the LRO Phase II (36.7% vs 11.8% P=0.008). A higher rate of laparoscopically assisted operations was implemented in LRO Phase II (53.3% vs 19.6% P=0.02). Tattooing was less frequently applied in Phase II (13.3% vs 37.3% P=0.021). Increased surgical competence was associated with the resection of a larger specimen in LRO (p<0.001). A longer follow-up duration was noted for the Phase I LRO patients (2 vs 0.27 months P=0.032).

CUSUM analysis of the postoperative complications in LCRO (Figure 7, P=0.48), LCO (Figure 8, P=0.419) and LRO (Figure 9, P=0.521), could not identify a LC. Correspondingly, no LC pattern was found in the open conversion rates of all study groups (Figure 10, P=0.3, Figure 11, P=0.8, Figure 12, P=0.19, respectively).

Finally, CUSUM analyses of the histopathological findings are displayed in the following figures. Considering the specimen length in LCO (Figure 13 and Figure 14), a decline until the 64th case (CL: 100%) was recognized. After this turning point, the specimen length steadily increases until the 99th case (CL: 94%), where it reaches a plateau. Similarly, in LRO (Figure 15 and Figure 16), the 47th case is the minimum CUSUM point of LRO specimen length. CPA results (Figure 17, 18, 19 and 20) regarding the lymph node yield did not reveal significant turning points.

Discussion

Summary of evidence

A learning curve is defined as the graphical representation of the variation of a surgeon's performance variable, plotted over a consecutive number of cases [53, 76]. Several techniques, such as group splitting, moving average and CUSUM analysis have been applied for the estimation of the learning curve [44, 45, 50, 51]. After an initial training period, the surgeon gradually undertakes more complex and challenging cases [90, 91]. The next step in this process is the attainment of mastery, where the further repetition of the tasks does not alter the perioperative outcomes and the LC reaches a plateau [45, 50, 69]. Therefore the key component in LC analysis is the identification of the exact turning points [77].

In addition to these, the innate learning variability between surgeons and the use of several clinical and pathologic characteristics as LC outcomes, are responsible for the variability in the reported LCRO LC results [43, 60]. More specifically, the current LCRO LC turning points range from 10 [50] to 200 cases [46].

The length of operative time has been extensively used as a primary LC analysis endpoint [50, 53, 76]. However, despite its universal acceptance, evaluation of a surgeon's experience based solely on operative time is prone to bias [53, 76]. More specifically, this indicator can be affected by the overlapping experience, case complexity and skill accumulation of assistants and theater nurses [39, 55, 76]. Although an operative plateau has been reported after 23 operations [41, 62], generally, over 96 cases are required for normalization of operative time [47]. This is in accordance with our findings, where the first phase of the LC was achieved at 110 LCROs.

A notable key point was the fact that the breakdown analyses of LCOs and LROs, estimated the LC turning points at 58 and 52 cases, respectively. The inconsistency with the pooled outcomes could be attributed to the incorporation of two surgery subgroups. Narrowing the analysis in a specific operation subtype lessens the LC, since a smaller number of learning steps are involved. On the contrary, even though laparoscopic skills may be transferrable, competence in LCRO requires expertise in both LCO and LRO. As so, the pooled LC represents a summation of the two individual LCs.

The limited field of view, the two-dimensional screen projection of anatomical structures and the use of fixed instrument ports increases the operative difficulty and thus, the risk of critical injuries [53]. Therefore an early LC completion was considered as an issue affecting patients' safety [37, 42, 45, 47]. Stabilization of the LCRO morbidity rate requires a significant case workload that spans from 140 to 200 patients [46, 47]. Interestingly, our data could not confirm the presence of an LC in perioperative morbidity. Similarly, in an analysis by MacKenzie et al., no LC trend was identified in morbidity, thus confirming an equivocal safety profile throughout the LC period [60]. However, these come in contrast with reports from substantially larger series and could possibly be the result of small sample size [37, 42, 45–47].

Conversion from laparoscopic to open surgery should be considered when after performing the expected processes the surgeon encounters a non-manageable situation [45, 50, 72]. This may include an intraoperative catastrophic event or the compromise of the oncological principles [41, 70, 72, 74]. Although it is not uniformly defined, conversion LC is estimated at the level of 61 cases, with further reduction once a systematic training protocol is applied [73, 77, 92]. Our conversion rates were within an acceptable range [47]. However, a conversion LC pattern was not confirmed in our study.

In oncological operations, besides perioperative efficiency results, certain specimen parameters should be considered [40, 43, 63]. Among them, lymph node yield is the most common, and as such, represents a prominent LC index [40, 43, 63]. However, such an approach can be misleading since the number of lymph nodes is only indicative of a formal oncological LCRO and can be affected by anthropometric and disease-related characteristics [93]. In our trial, an LC pattern in lymph node yield was identified without, though, confirming a significant turning point. Moreover, CPA analysis of the specimen length reported wider resections after the 64th and 47th cases in LCO and LRO, respectively. We did not use the R1 status as an LC endpoint, due to its very low frequency. In our study, the CME/ TME violation rate was not submitted to a LC analysis for two reasons. First, in such a case, the operation was converted in order to secure adherence to the oncologic principles. Secondly, the rates of pathologically confirmed non-CME/ TME dissection planes were low, thus inhibiting any further analysis.

Therefore, in order to exploit the benefits of LCRO, a faster surpassing of the LC is required [53]. Modular training facilitates the breakdown of the operation in sequential tasks that require optimization and evaluation by a dedicated proctor [73]. The addition of specialized courses, observation of competent mentor techniques and exposure in a specific operational volume resulted in a significant LC reduction [73, 76]. These approaches have been successfully encompassed in several nationwide structured training programs, with apparently successful results [45, 77]. However, this is not the case for the majority of surgeons, especially in health systems that have not incorporated LCRO in their officially training algorithms [42]. As so, in such settings the implementation of LCRO relies on the individual learning efforts of the involved surgeons, with questionable outcomes.

In this trial the combined LC of two staff surgeons was analyzed. Training was not based on a structured program and featured attendance to courses and expert guidance. It must be noted, though that the prior competence in minimal invasive surgery and open colorectal resections may have accelerated overall LC. As a result these findings may not reflect the learning slope of a typical surgical trainee.

Before appraising the results of our study, several limitations should be considered. First of all, despite the fact that the turning points provided by our analyses were statistically significant, our trial included a relatively small sample size. This prevented us from performing further analyses regarding the possible affecting factors and, subsequently risk-adjusting the LCs. Since we attempted to provide an overall evaluation of the colorectal LCs, the inherent heterogeneity of the patient and operative characteristics reduces the validity of our findings.

Additionally, the retrospective design of our trial further contributes to the total amount of bias. Finally, the fact that only two operating surgeons were involved in this study, inhibits the safe extrapolation of these results to a wider sample of consultants and surgical residents.

Conclusions

Overall, our study concluded that, in terms of operative time, the LC of a dedicated colorectal surgical team in LCRO consisted of 3 phases. The CPA analysis identified the 110th case as the separation key-point of the first two phases. A plateau was reached after the 145th case. Subgroup analysis of the LCO and LRO estimated the 58th and 52nd case as the turning points, respectively. Although we were able to confirm the presence of an LC pattern in the histopathological endpoints, this was not the case for the open conversion and morbidity outcomes. The LC in the absence of a formal training program validates the comparability of the perioperative outcomes, even in the initial learning phases. However, such initiatives are necessary for the safe and efficient implementation of LCROs

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Appendix

Tables

		Total	*Colon Operations*	*Rectal Operations*	*P*
N		214	133	81	
Sex	Male	128(59.8%)	78(58.6%)	50(61.7%)	NS
	Female	86(40.2%)	55(41.4%)	31(38.3%)	
Age (years)		70(13)	71(14)	68(13)	NS
BMI (kg/m^2)		27(5)	28(5)	26.5(4)	NS
ASA score	I	71(33.2%)	35(26.3%)	36(44.4%)	0.021
	II	117(54.7%)	79(59.4%)	38(46.9%)	
	III	26(12.1%)	19(14.3%)	7(8.6%)	
Diagnosis	Malignancy	206(96.3%)	125(94%)	81(100%)	NS
	Diverticulitis	6(2.8%)	6(4.5%)	0(0%)	
	Volvulus	1(0.5%)	1(0.8%)	0(0%)	
	Crohn's disease	1(0.5%)	1(0.8%)	0(0%)	
Previous operation		17(7.9%)	13(9.8%)	4(4.9%)	NS
T	1	51(24.8%)	33(26.4%)	18(22.2%)	NS
	2	63(30.6%)	39(31.2%)	24(29.6%)	
	3	85(41.3%)	47(37.6%)	38(46.9%)	
	4	7(3.4%)	6(4.8%)	1(1.2%)	
N	0	153(74.3%)	89(71.2%)	64(79%)	NS
	1	42(20.4%)	30(24%)	12(14.8%)	
	2	11(5.3%)	6(4.8%)	5(6.2%)	
M	0	205(99.5%)	125(100%)	80(98.8%)	NS
	1	1(0.5%)	0(0%)	1(1.2%)	
Neoadjuvant modality		19(9.2%)	2(1.6%)	17(20%)	<0.001
Operation	Right colectomy	76(35.5%)	76(57.1%)	-	<0.001
	Left colectomy	31(14.5%)	31(23.3%)	-	
	Sigmoidectomy	26(12.1%)	26(19.5%)	-	
	Low anterior resection	72(33.6%)	-	72(88.9%)	
	Ultra low anterior resection	7(3.3%)	-	7(8.6%)	
	Abdominoperineal resection	2(1%)	-	2(2.4%)	
Emergency status	Elective	212(99.1%)	131(98.5%)	81(100%)	NS
	Semi-elective	2(0.9%)	2(1.5%)	0(0%)	
Laparoscopic approach	Totally laparoscopic	182(85%)	127(95.5%)	55(67.9%)	<0.001
	Laparoscopy assisted	32(15%)	6(4.5%)	26(32.1%)	
Preoperative optimization	Bowel preparation	191(89.3%)	112(84.2%)	79(97.5%)	0.002
	Antibiotic preparation	206(96.3%)	127(95.5%)	79(97.5%)	NS
	Tattoo	51(23.8%)	28(21.1%)	23(28.4%)	NS
Extraction site	Pfannenstiel	95(44.4%)	40(30.1%)	55(67.9%)	<0.001
	Subumbilical	19(8.9%)	4(3%)	15(18.5%)	
	Transumbilical	100(46.7%)	89(66.9%)	11(13.6%)	
Anastomosis	Stapled	159(75%)	80(60.2%)	79(100%)	<0.001
	Handsewn	53(25%)	53(39.8%)	0(0%)	
	Intracorporeal	112(52.8%)	50(37.6%)	62(78.4%)	<0.001
	Extracorporeal	100(47.1%)	83(62.4%)	17(21.5%)	
	Protective stoma	66(30.8%)	9(6.8%)	57(70.4%)	<0.001
Operation duration (min)		180(51)	180(50)	200(60)	<0.001
Open conversion		20(9.3%)	6(4.5%)	14(17.3%)	0.002
Transfusion		8(3.7%)	4(3%)	4(4.9%)	NS
Tumor diameter (cm)		3(2.2)	3(2)	3.75(2.5)	NS
Specimen length (cm)		20(9)	21(7)	15(7)	<0.001
Distal margin (cm)		5(4.35)	5.25(3.5)	4.5(4.25)	0.01
Lymph nodes		17(12)	19(13)	15(11)	0.004

Lymph nodes ratio		0(2.3)	0(4)	0(0)	NS
Histological grade	1	40(19.4%)	20 (16%)	20(24.7%)	NS
	2	135(65.5%)	89(71.2%)	46(56.8%)	
	3	31(15%)	16(12.8%)	15(18.5%)	
R status	0	204(95.3%)	124(99.2%)	80(98.8%)	NS
	1	2(0.9%)	1(0.8%)	1(1.2%)	
Resection Plane	Mesocolic/ Mesorectal	183(88.8%)	108(86.4%)	75(88.8%)	NS
	Intramesocolic/ Intramesorectal	19(9.2%)	14(11.2%)	5(6.2%)	
	Muscularis Propria	4(1.9%)	3(2.4%)	1(1.2%)	
Extramural vascular invasion		54(26.2%)	33(26.4%)	21(25.9%)	NS
Perineural invasion		21(10.2%)	13(10.4%)	8(9.9%)	NS
Mucous	Foci	29(14.1%)	20(16%)	9(11.1%)	NS
	Diffuse	20(9.7%)	15(12%)	5(6.2%)	
Complications	Total	49(22.9%)	33(24.8%)	16(19.8%)	NS
	Wound infection	9(4.2%)	5(3.8%)	4(4.9%)	NS
	Wound dehiscence	2(0.9%)	2(1.5%)	0(0%)	
	Leak	14(6.5%)	10(7.5%)	4(4.9%)	
	Postoperative ileus	11(5.1%)	8(6%)	3(3.7%)	
	Urinary tract infection	2(0.9%)	0(0%)	2(2.5%)	
	Urinary retention	2(0.9%)	1(0.8%)	1(1.2%)	
	Bleeding	3(1.4%)	1(0.8%)	2(2.5%)	
	Pulmonary embolism	2(0.9%)	2(1.5%)	0(0%)	
	ARDS	1(0.5%)	0(0%)	1(1.2%)	
	Other	4(1.9%)	4(3%)	0(0%)	
Relaparotomy		11(5.1%)	8(6%)	3(3.7%)	NS
ICU		8(3.7%)	5(3.8%)	3(3.7%)	NS
Mortality		5(2.3%)	4(3%)	1(1.2%)	NS
Length of hospital stay (days)		6(2)	6(2)	6(2)	NS
Follow up (months)		2(3.75)	2(5.8)	2(2.5)	NS

Table 1. Patient Characteristics

	Overall				**Colon**				**Rectal**		
	Spearman's P	*Subgroups*	*Operation Duration*		*Spearman's P*	*Subgroups*	*Operation Duration*		*Spearman's P*	*Subgroups*	*Operation Duration*
Sex	0.002	Male	192.5(49)	**Sex**	0.015	Male	180(40)	**Sex**	0.015	Male	205(50)
		Female	180(50)			Female	160(40)			Female	180(40)
Diagnosis	0.01	Malignancy	180(50)	**Diagnosis**	0.04	Malignancy	180(50)	**Laparoscopic approach**	0.005	Totally laparoscopic	200(40)
		Diverticulitis	160(33)			Diverticulitis	160(33)			Laparoscopy assisted	220(50)
Distance from anal verge (cm)	<0.001			**Laparoscopic approach**	0.001	Totally laparoscopic	180(45)	**Neoadjuvant modality**	0.006	Yes	220(75)
Operation	0.001	Right colectomy	180(50)			Laparoscopy assisted	240(70)			No	200(54)
		Left colectomy	160(40)	**Neoadjuvant modality**	0.02	Yes	250	**Tattoo**	0.001	Yes	180(45)
		Sigmoidectomy	180(60)			No	180(50)			No	210(60)
		Low anterior resection	200(50)	**Tumor diameter (cm)**	0.006			**Protective stoma**	<0.001	Yes	210(40)
		Ultra low anterior resection	240(50)	**Histology specimen length (cm)**	0.001					No	160(44)
Laparoscopic approach	<0.001	Totally laparoscopic	180(50)								
		Laparoscopy assisted	230(50)								
Neoadjuvant modality	<0.001	Yes	240(60)								
		No	180(50)								
Tattoo	0.023	Yes	180(50)								
		No	180(50)								

Extraction site	0.005	Pfannenstiel	190(60)		
		Subumbilical	200(60)		
		Transumbilical	180(50)		
Stapled/Handsewn Anastomosis	0.04	Stapled	190(50)		
		Handsewn	180(50)		
Intra/Extracorporeal	0.048	Intracorporeal	190(50)		
		Extracorporeal	180(50)		
Protective stoma	<0.001	Yes	210(50)		
		No	180(49)		
Tumor diameter (cm)	0.014				

Table 2. Correlation of perioperative characteristics to LCRO operation duration using Spearman's Rank-Order test.

		Overall				**Colon**			**Rectal**		
		Phase I (1-109)	*Phase II (110-144)*	*Phase III (145-214)*	*P*	*Phase I (1-57)*	*Phase II (58-133)*	*P*	*Phase I (1-51)*	*Phase II (52-81)*	*P*
N		109	35	70		57	76		51	30	
Sex	Male	68(62.4%)	24(68.6%)	36(51.4%)	NS	37(64.9%)	41(53.9%)	NS	30(58.8%)	20(66.7%)	NS
	Female	41(37.6%)	11(31.4%)	34(48.6%)		20(35.1%)	35(46.1%)		21(41.2%)	10(33.3%)	
Age (years)		71.5(12)	70(13)	69.5(14)	NS	72(14)	71(13)	NS	69.5(12)	67(16)	NS
BMI (kg/m^2)		27(5)	28(4)	27(5)	NS	28(6)	28(5)	NS	26(3)	27.5(6)	NS
ASA score	I	36(33%)	13(37.1%)	22(31.4%)		14(24.6%)	21(27.6%)	NS	21(41.2%)	15(50%)	
	II	62(56.9%)	16(45.7%)	39(55.7%)	NS	35(61.4%)	44(57.9%)		27(52.9%)	11(36.7%)	NS
	III	11(10.1%)	6(17.1%)	9(12.9%)		8(14%)	11(14.5%)		3(5.9%)	4(13.3%)	
Diagnosis	Malignancy	106(97.2%)	34(97.1%)	66(94.3%)		54(94.7%)	71(93.4%)	NS	51(100%)	30(100%)	-
	Diverticulitis	2(1.8%)	1(2.9%)	3(4.3%)	NS	2(3.5%)	4(5.3%)		-	-	
	Volvulus	1(0.9%)	0(0%)	0(0%)		1(1.8%)	0(0%)		-	-	
	Crohn's disease	0(0%)	0(0%)	1(1.4%)		0(0%)	1(1.3%)		-	-	
Previous operation		13(11.9%)	2(5.7%)	2(2.9%)	NS	9(15.8%)	4(5.3%)	0.04	4(7.8%)	0(0%)	NS
T	1	24(22.6%)	6(17.6%)	21(31.8%)	NS	12(22.6%)	21(29.2%)	NS	12(23.5%)	6(20%)	NS
	2	34(32.1%)	7((20.6%)	22(33.3%)		16(30.2%)	23(31.9%)		18(35.3%)	6(20%)	
	3	43(40.6%)	20(58.8%)	22(33.3%)		21(39.6%)	26(36.1%)		20(39.2%)	18(60%)	
	4	5(4.7%)	1(2.9%)	1(1.5%)		4(7.5%)	2(2.8%)		1(2%)	0(0%)	
N	0	77(74.5%)	25(73.5%)	49(74.2%)	NS	36(67.9%)	53(73.6%)	NS	41(80.4%)	23(76.7%)	
	1	23(21.7%)	6(17.6%)	13(19.7%)		16(30.2%)	14(19.4%)		6(13.7%)	5(16.7%)	NS
	2	4(3.8%)	3(8.8%)	4(6.1%)		1(1.9%)	5(6.9%)		3(5.9%)	2(6.7%)	
M	0	106(100%)	34(100%)	65(98.5%)	NS	53(100%)	72(100%)	-	51(100%)	29(96.7%)	NS
	1	0(0%)	0(0%)	1(1.5%)		-	-		0(0%)	1(3.3%)	
Neoadjuvant modality		6(5.5%)	5(14.3%)	8(11.4%)	NS	0(0%)	2(2.6%)	NS	6(11.8%)	11(36.7%)	0.008
Operation	Right colectomy	34(31.2%)	13(37.1%)	29(41.4%)	NS	34(59.6%)	42(55.3%)	NS	-	-	NS
	Left colectomy	10(9.2%)	6(17.1%)	15(21.4%)		10(17.5%)	21(27.6%)		-	-	
	Sigmoidectomy	13(11.9%)	2(5.7%)	11(15.7%)		13(22.8%)	13(17.1%)		-	-	
	Low anterior resection	46(42.2%)	13(37.1%)	13(18.6%)		-	-		45(88.2%)	27(90%)	

	Ultra low anterior resection	4(3.7%)	1(2.9%)	2(2.9%)		-	-		4(7.8%)	3(10%)	
	Abdominoperineal resection	2(1.8%)	0(0%)	0(0%)		-	-		2(4%)	0(0%)	
Emergency status	Elective	109(100%)	35(100%)	68(97.1%)	NS	57(100%)	74(97.4%)	NS	51(100%)	30(100%)	-
	Semi-elective	0(0%)	0(0%)	2(2.9%)		0(0%)	2(2.6%)		-	-	
Laparoscopic approach	Totally laparoscopic	98(89.9%)	24(68.6%)	60(85.7%)	0.009	56(98.2%)	71(93.4%)	NS	41(80.4%)	14(46.7%)	0.002
	Laparoscopy assisted	11(10.1%)	11(31.4%)	10(14.3%)		1(1.8%)	5(6.6%)		10(19.6%)	16(53.3%)	
Preoperative optimization	Bowel preparation	107(98.2%)	30(85.7%)	54(77.1%)	<0.001	56(98.2%)	56(73.7%)	<0.001	50(98%)	29(96.7%)	NS
	Antibiotic preparation	105(96.3%)	33(94.3%)	68(97.1%)	NS	54(94.7%)	73(96.1%)	NS	50(98%)	29(96.7%)	NS
	Tattoo	36(33%)	2(5.7%)	13(18.6%)	0.002	17(29.8%)	11(14.5%)	0.032	19(37.3%)	4(13.3%)	0.021
Extraction site	Pfannenstiel	52(47.7%)	15(42.9%)	28(40%)	NS	15(26.3%)	25(32.9%)	NS	37(72.5)	18(60%)	NS
	Subumbilical	12(11%)	4(11.4%)	3(4.3%)		2(3.5%)	2(2.6%)		9(17.6%)	6(20%)	
	Transumbilical	45(41.3%)	16(45.7%)	39(55.7%)		40(70.2%)	49(64.5%)		5(9.8%)	6(20%)	
Anastomosis	Stapled	85(78.7%)	24(70.6%)	50(71.4%)	NS	34(59.6%)	46(60.5%)	NS	50(100%)	29(100%)	NS
	Handsewn	23(21.3%)	10(29.4%)	20(28.6%)		23(40.4%)	30(39.5%)		0(0%)	0(0%)	
	Intracorporeal	57(52.8%)	16(47.1%)	39(55.7%)	NS	18(31.6%)	32(42.1%)	NS	38(76%)	24(82.8%)	NS
	Extracorporeal	51(47.2%)	18(52.9%)	31(44.3%)		39(68.4%)	44(57.9%)		12(24%)	5(17.2%)	
	Protective stoma	38(34.9%)	11(31.4%)	17(24.3%)	NS	3(5.3%)	6(7.9%)	NS	34(66.7%)	23(76.7%)	NS
Operation duration (min)		180(50)	220(60)	180(40)	<0.001	160(48)	180(40)	0.003	200(50)	220(63)	0.003
Open conversion		13(11.9%)	2(5.7%)	5(7.1%)	NS	4(7%)	2(2.6%)	NS	8(15.7%)	6(20%)	NS
Transfusion		5(4.6%)	0(0%)	3(4.3%)	NS	3(5.3%)	1(1.3%)	NS	1(2%)	3(10%)	NS
Tumor diameter (cm)		3(2.1)	4(2.4)	3(2)	NS	3(1.5)	3.5(2)	NS	4(2.4)	3(3)	NS
Specimen length (cm)		16.25(7.25)	22.5(6.5)	24(8)	<0.001	20.5(8)	23(8.75)	0.001	14.25(3.75)	21(6)	<0.001
Distal margin (cm)		4(3.5)	7(2)	7(5)	<0.001	4(2.5)	7(3.5)	<0.001	4(4.25)	5(4.5)	NS
Lymph nodes		15(10)	20(19)	21(12)	0.016	15(10)	22(13)	0.002	15(10)	12.5(15)	NS
Lymph node ratio		0(0)	0(0.8)	0(8)	NS	0(4.5)	0(3.8)	NS	0(0)	0(13.5)	NS
Histological grade	1	26(24.5%)	1(2.9%)	13(19.7%)	0.013	10(18.9%)	10(13.9%)	0.009	16(31.4%)	4(13.3%)	NS
	2	60(56.6%)	27(79.5%)	48(72.7%)		31(58.5%)	58(80.6%)		27(52.9%)	19(63.3%)	
	3	20(18.9%)	6(17.6%)	5(7.6%)		12(22.6%)	4(5.6%)		8(15.7%)_	7(23.3%)	

R status	0	105(99.1%)	33(97.1%)	66(100%)	NS	53(98.1%)	71(100%)	NS	51(100%)	29(96.7%)	
	1	1(0.9%)	1(2.9%)	0(0%)		1(1.9%)	0(0%)		0(0%)	1(3.3%)	NS
Resection Plane	Mesocolic/ Mesorectal	91(85.8%)	31(91.2%)	61(92.4%)	NS	43(79.6%)	65(91.5%)	NS	47(92.2%)	28(93.3%)	NS
	Intramesocolic/ Intramesorectal	12(11.3%)	3(8.8%)	4(6.1%)		9(16.7%)	5(7%)		3(5.9%)	2(6.7%)	
	Muscularis Propria	3(2.8%)	0(0%)	1(1.5%)		2(3.7%)	1(1.4%)		1(2%)	0(0%)	
Extramural vascular invasion		30(28.3%)	7(20.6%)	17(25.8%)	NS	13(24.5%)	20(27.8%)	NS	16(31.4%)	5(16.7%)	NS
Perineural invasion		13(12.3%)	4(11.8%)	4(6.1%)	NS	7(13.2%)	6(8.3%)	NS	6(11.8%)	2(6.7%)	NS
Mucous	Foci	11(10.4%)	12(35.3%)	6(9.1%)	0.006	6(11.3%)	14(19.4%)	NS	4(7.8%)	5(16.7%)	NS
	Diffuse	9(8.5%)	3(8.8%)	8(12.1%)		7(13.2%)	8(11.1%)		2(3.9%)	3(10%)	
Complications	Total	28(25.7%)	9(25.7%)	12(17.1%)	NS	15(26.3%)	18(23.7%)	NS	12(23.5%)	4(13.3%)	NS
	Wound infection	5(4.6%)	2(5.7%)	2(2.9%)	NS	1(1.8%)	4(5.3%)	NS	4(7.8%)	0(0%)	NS
	Wound dehiscence	1(0.9%)	1(2.9%)	0(0%)		1(1.8%)	1(1.3%)		0(0%)	0(0%)	
	Leak	8(7.3%)	4(11.4%)	2(2.9%)		5(8.8%)	5(6.6%)		2(3.9%)	2(6.7%)	
	Postoperative ileus	7(6.4%)	1(2.9%)	3(4.3%)		4(7%)	4(5.3%)		3(5.9%)	0(0%)	
	Urinary tract infection	2(1.8%)	0(0%)	0(0%)		0(0%)	0(0%)		2(3.9%)	0(0%)	
	Urinary retention	1(0.9%)	0(0%)	1(1.4%)		0(0%)	1(1.3%)		1(2%)	0(0%)	
	Bleeding	1(0.9%)	0(0%)	2(2.9%)		0(0%)	1(1.3%)		1(2%)	1(3.3%)	
	Pulmonary embolism	1(0.9%)	1(2.9%)	0(0%)		1(1.8%)	1(1.3%)		0(0%)	0(0%)	
	ARDS	0(0%)	0(0%)	1(1.4%)		0(0%)	0(0%)		0(0%)	1(3.3%)	
	Other	3(2.8%)	0(0%)	1(1.4%)		3(5.3%)	1(1.3%)		0(0%)	0(0%)	
Relaparotomy		5(4.6%)	3(8.6%)	3(4.3%)	NS	2(3.5%)	6(7.9%)	NS	2(3.9%)	1(3.3%)	NS
ICU		6(5.5%)	1(2.9%)	1(1.4%)	NS	4(7%)	1(1.3%)	NS	2(3.9%)	1(3.3%)	NS
Mortality		4(3.7%)	1(2.9%)	0(0%)	NS	3(5.3%)	1(1.3%)	NS	1(2%)	0(0%)	NS
Length of hospital stay (days)		6(2)	6(3)	6(2)	NS	6(2)	6(2)	NS	6(2)	5(1)	NS
Follow up (months)		2(3.25)	0.65(0)	6(5)	NS	2(3.3)	6.8(4.4)	NS	2(3)	0.27(0)	0.032

Table 3. Patient characteristics on the different phases of the learning curves

Figures

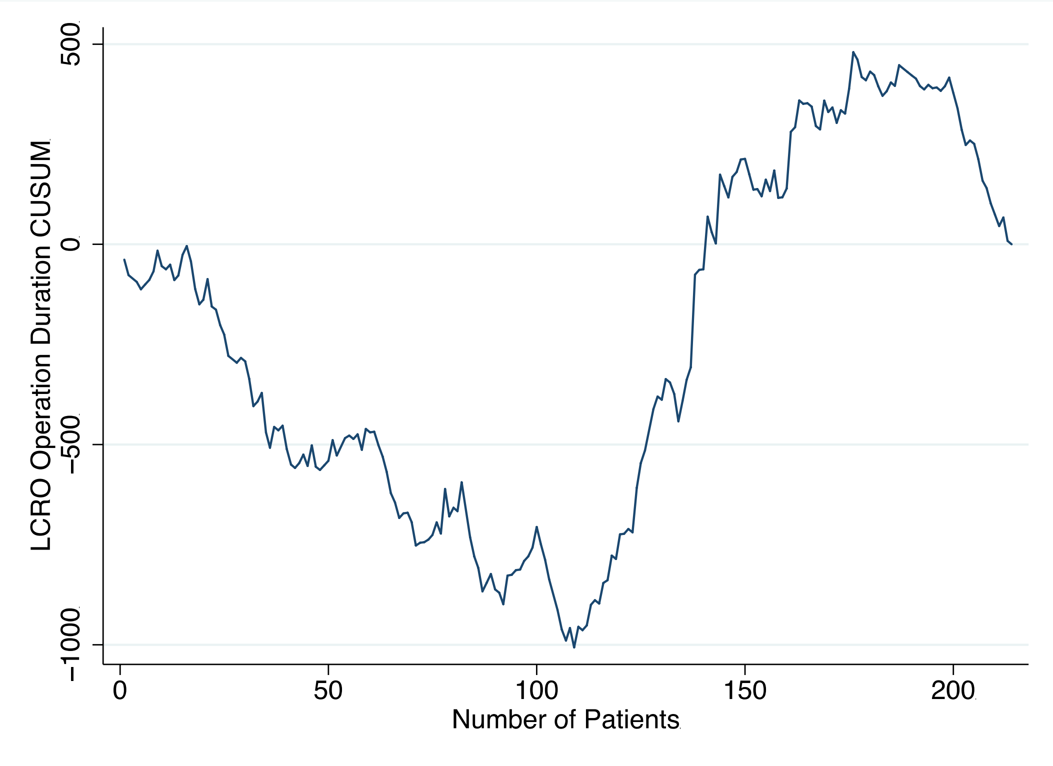

Figure 1. CUSUM analysis of operation duration in laparoscopic colorectal operations

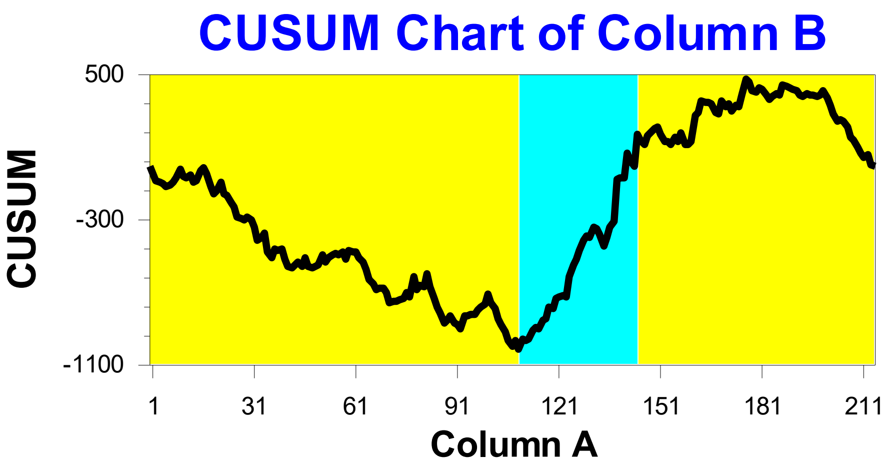

Figure 2. LCRO operation duration CPA analysis

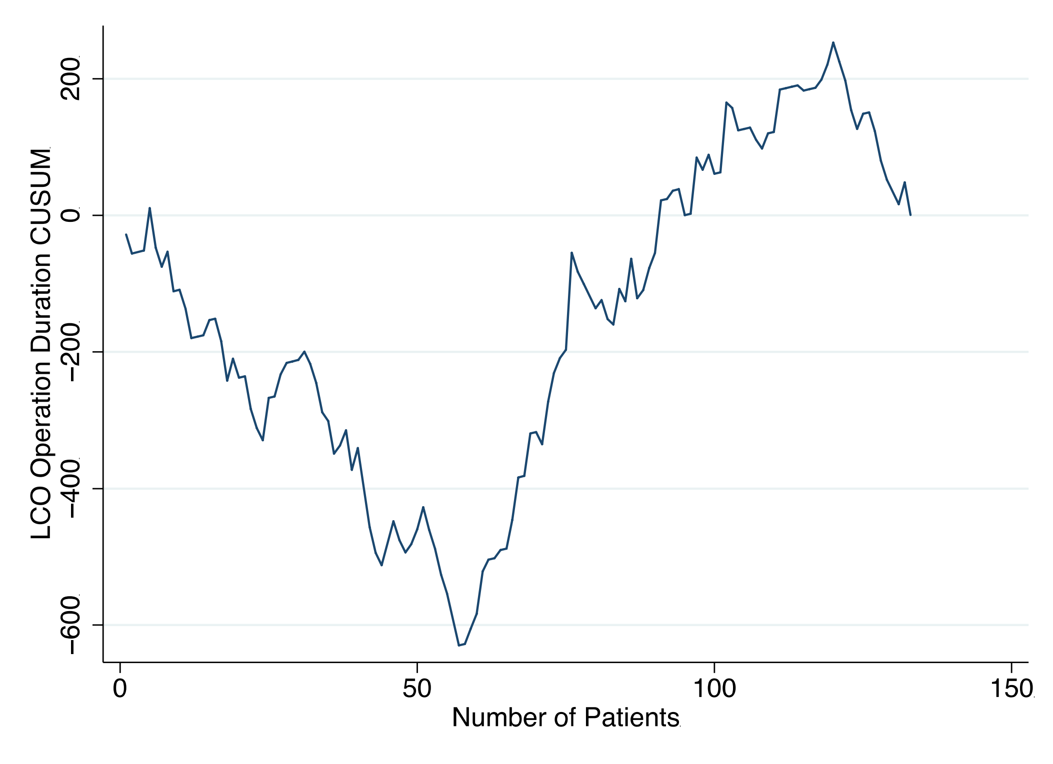

Figure 3. CUSUM analysis of operation duration in laparoscopic colon operations

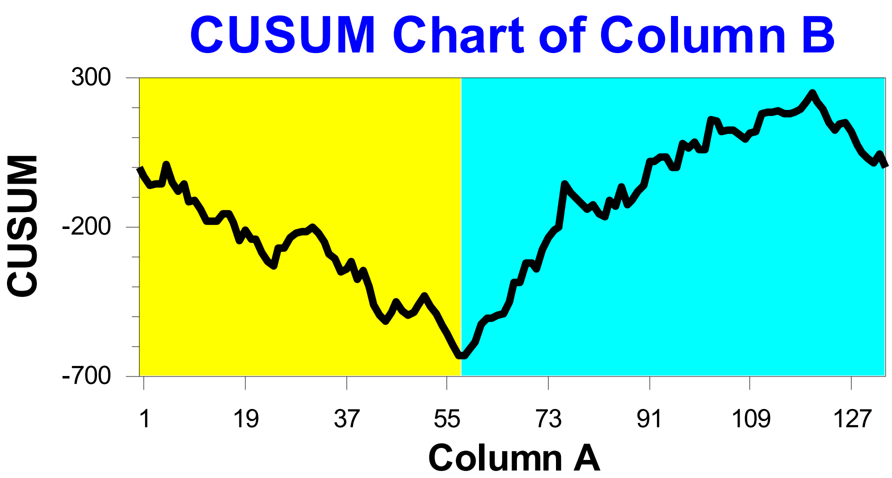

Figure 4. LCO operation duration CPA analysis

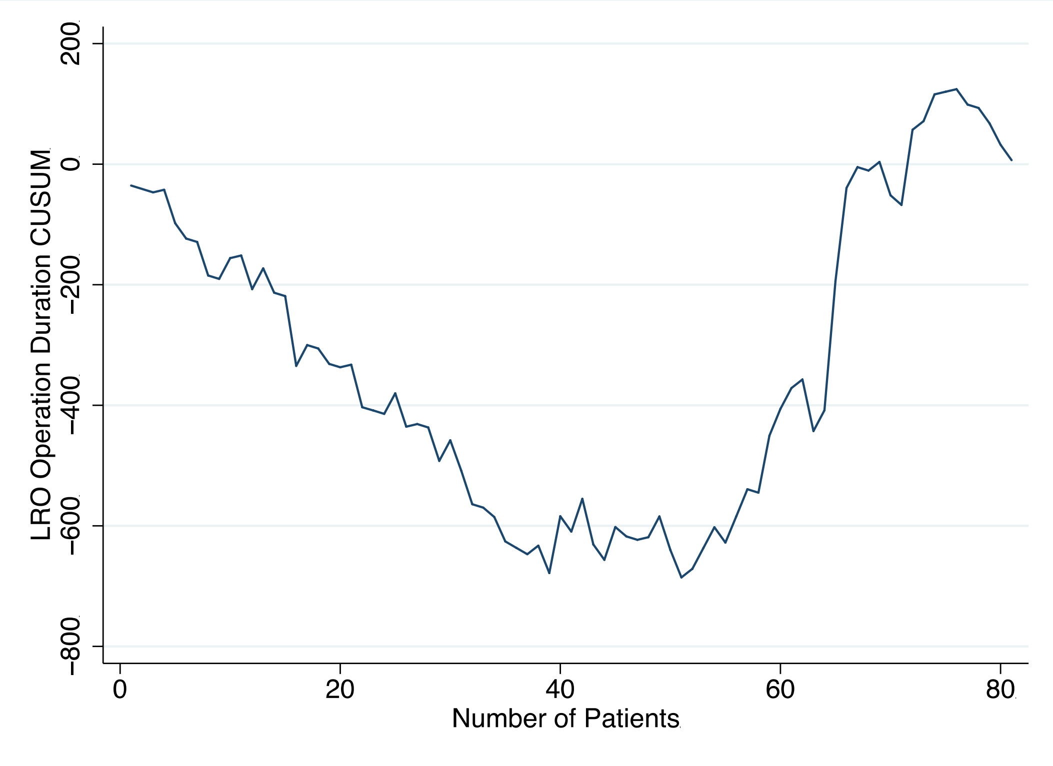

Figure 5. CUSUM analysis of operation duration in laparoscopic rectal operations

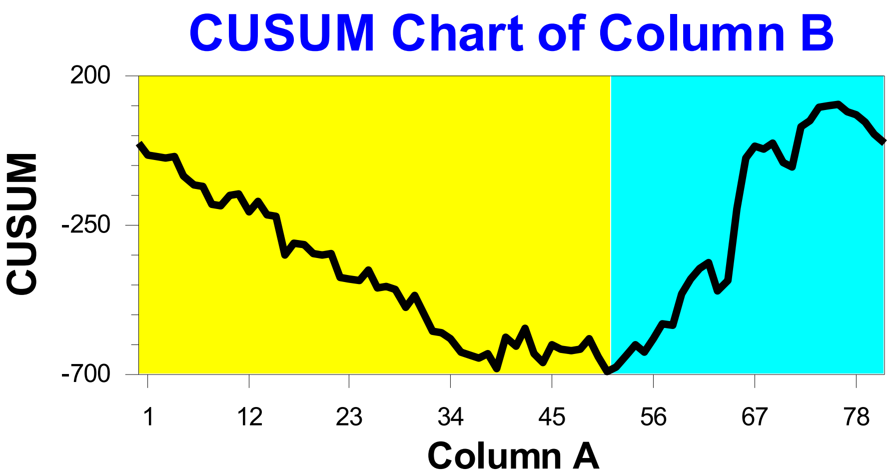

Figure 6. LRO operation duration CPA analysis

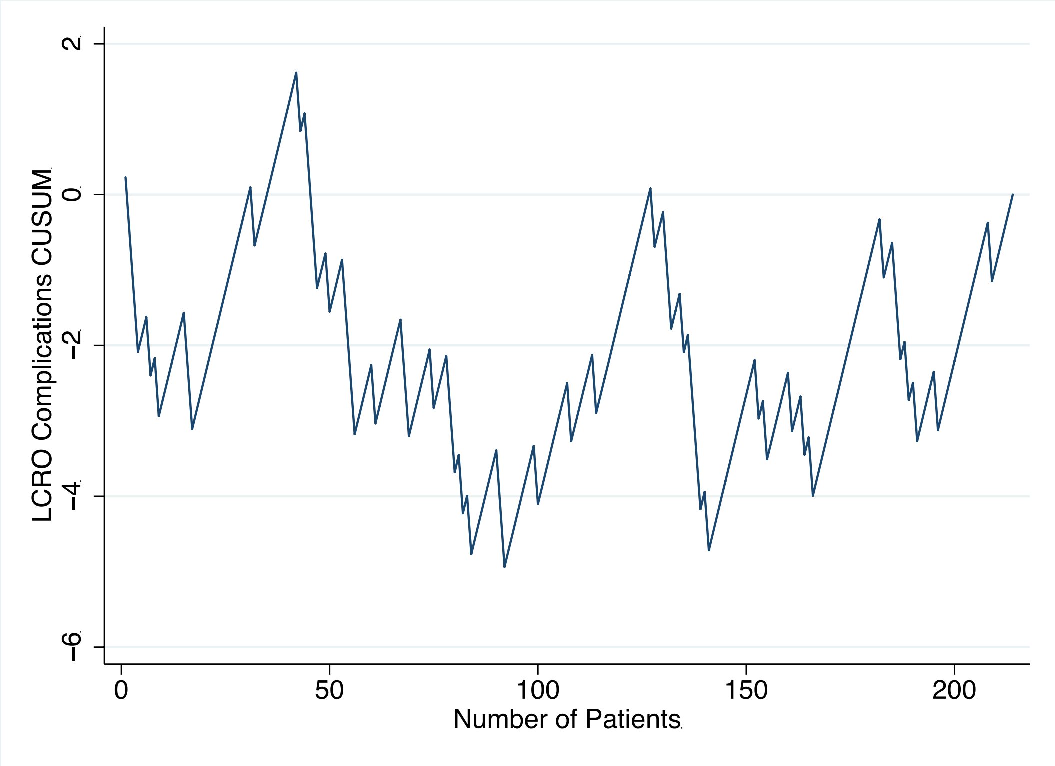

Figure 7. LCRO complication rate CUSUM analysis

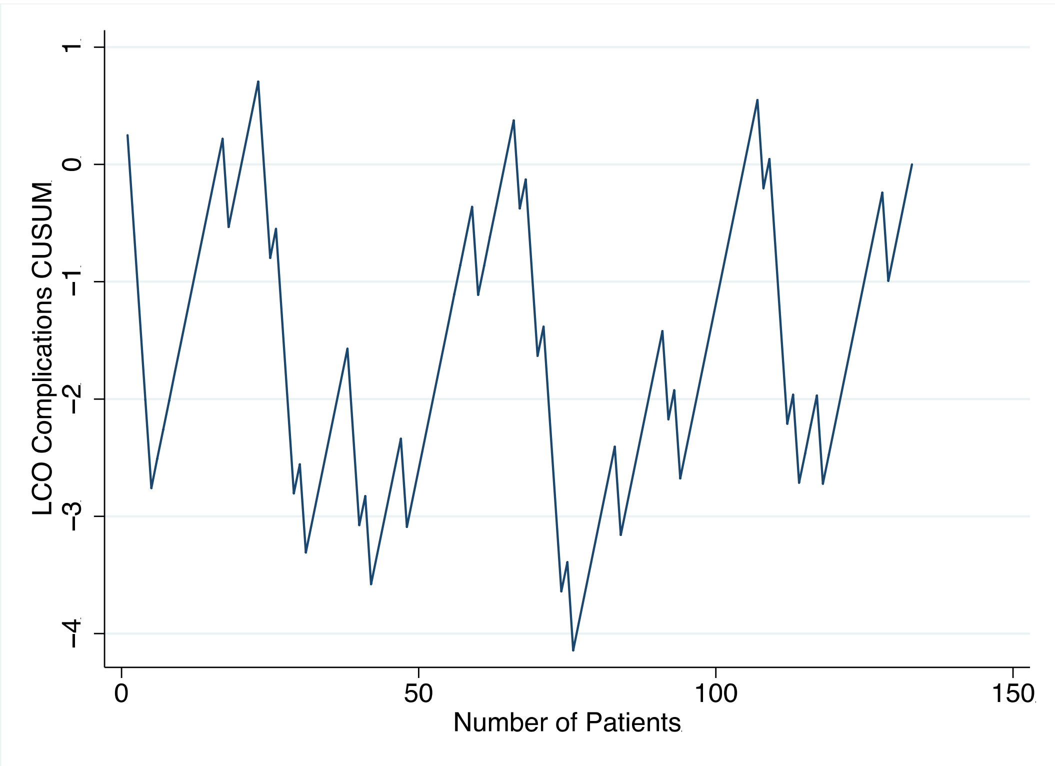

Figure 8. LCO complication rate CUSUM analysis

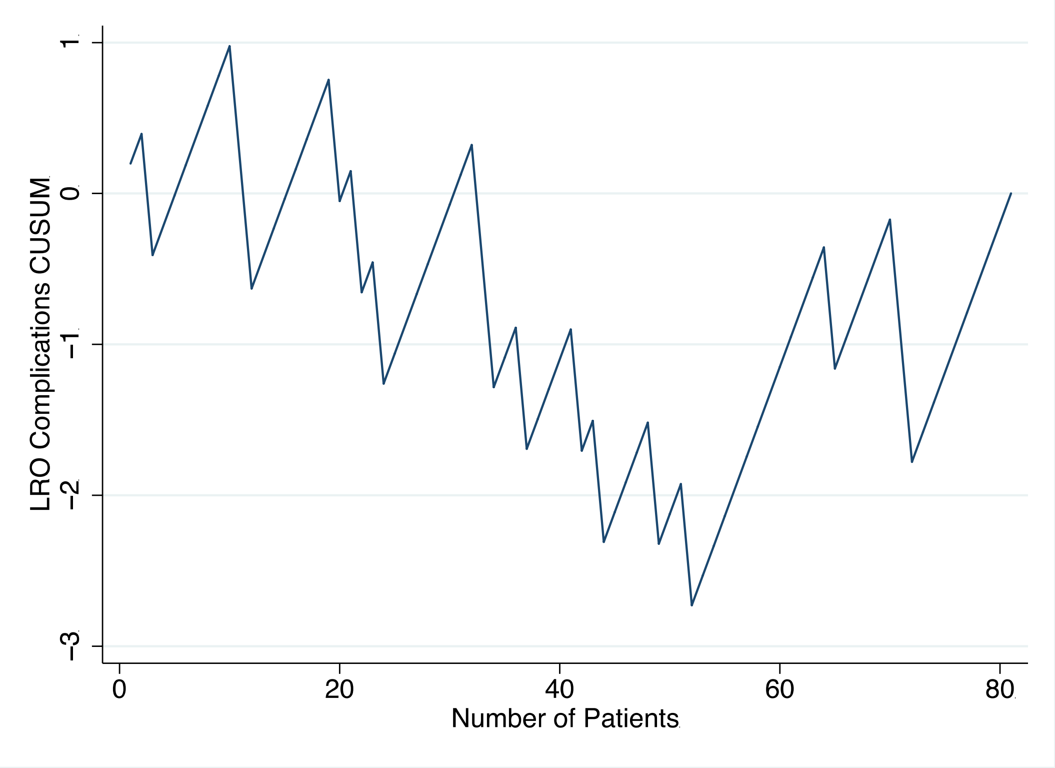

Figure 9. LRO complication rate CUSUM analysis

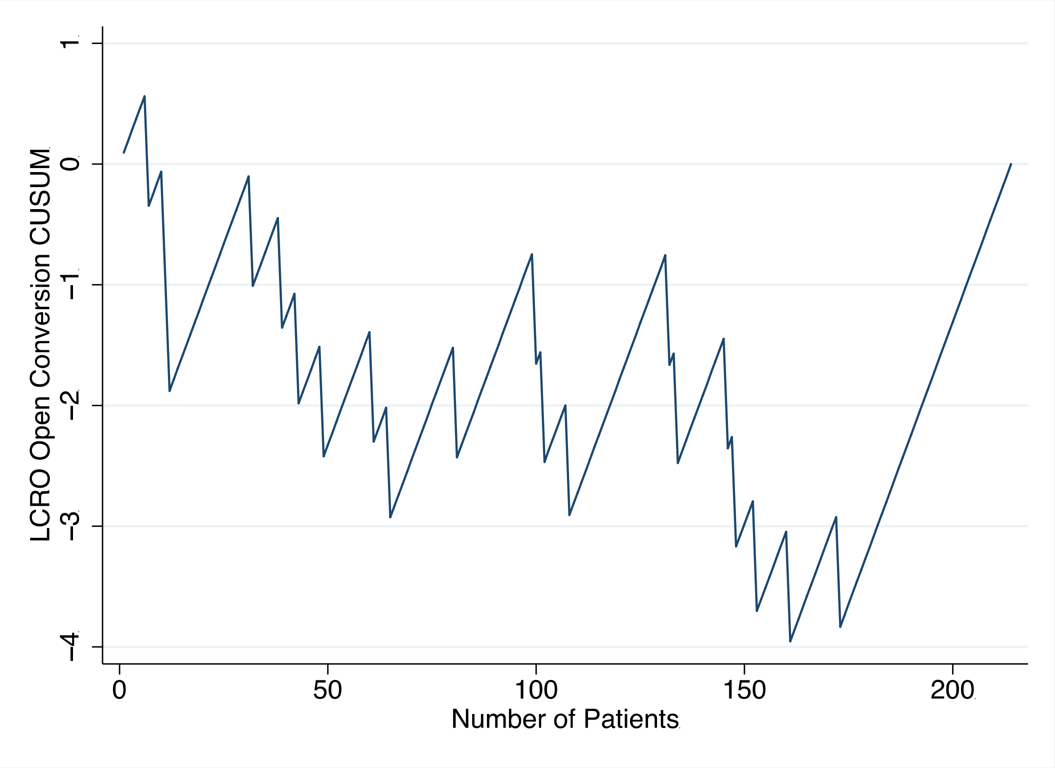

Figure 10. LCRO open conversion rate CUSUM analysis

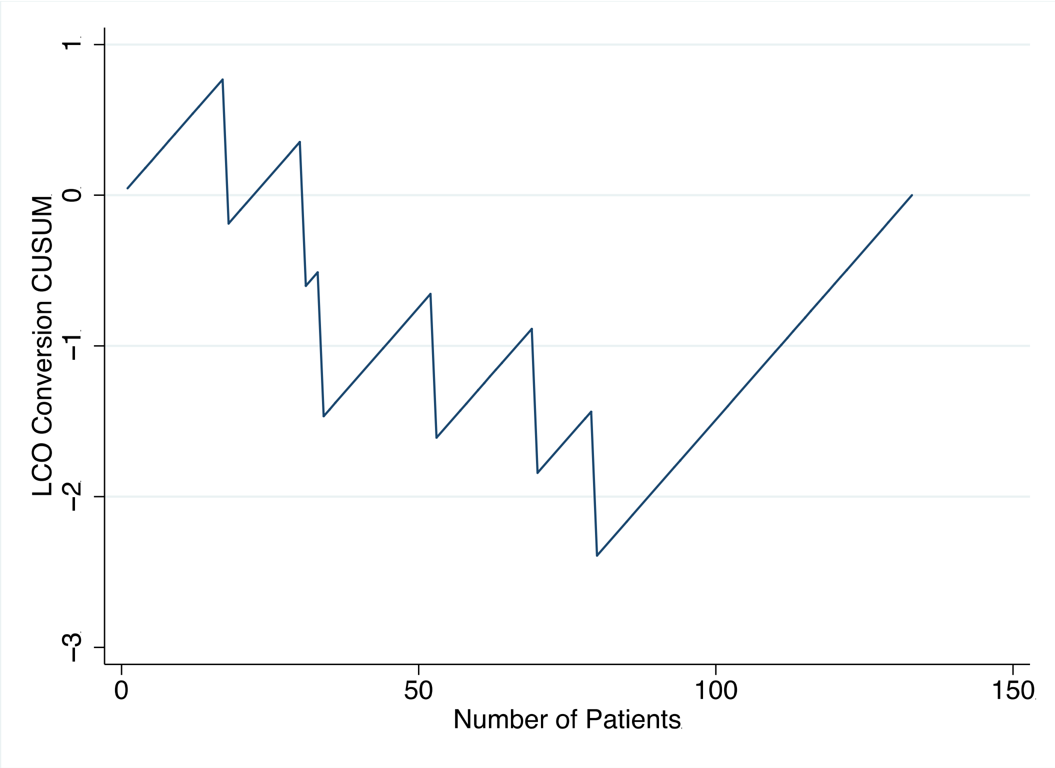

Figure 11. LCO open conversion rate CUSUM analysis

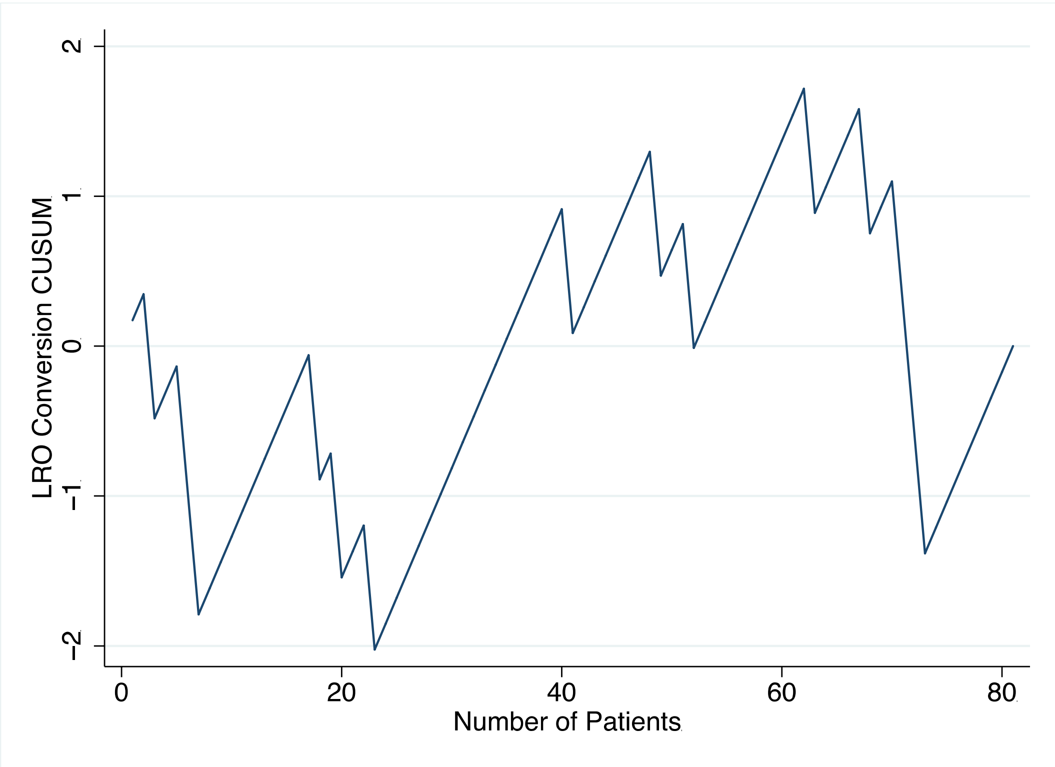

Figure 12. LRO open conversion rate CUSUM analysis

Figure 13. LCO specimen length CUSUM analysis

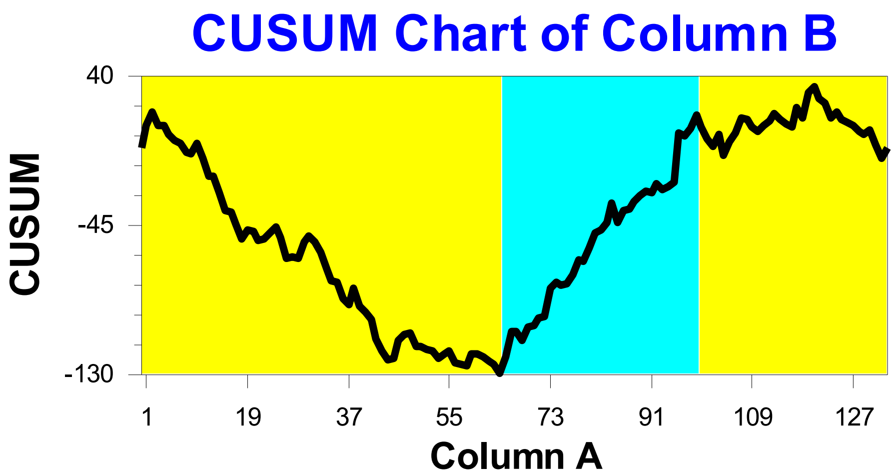

Figure 14. LCO specimen length CPA analysis

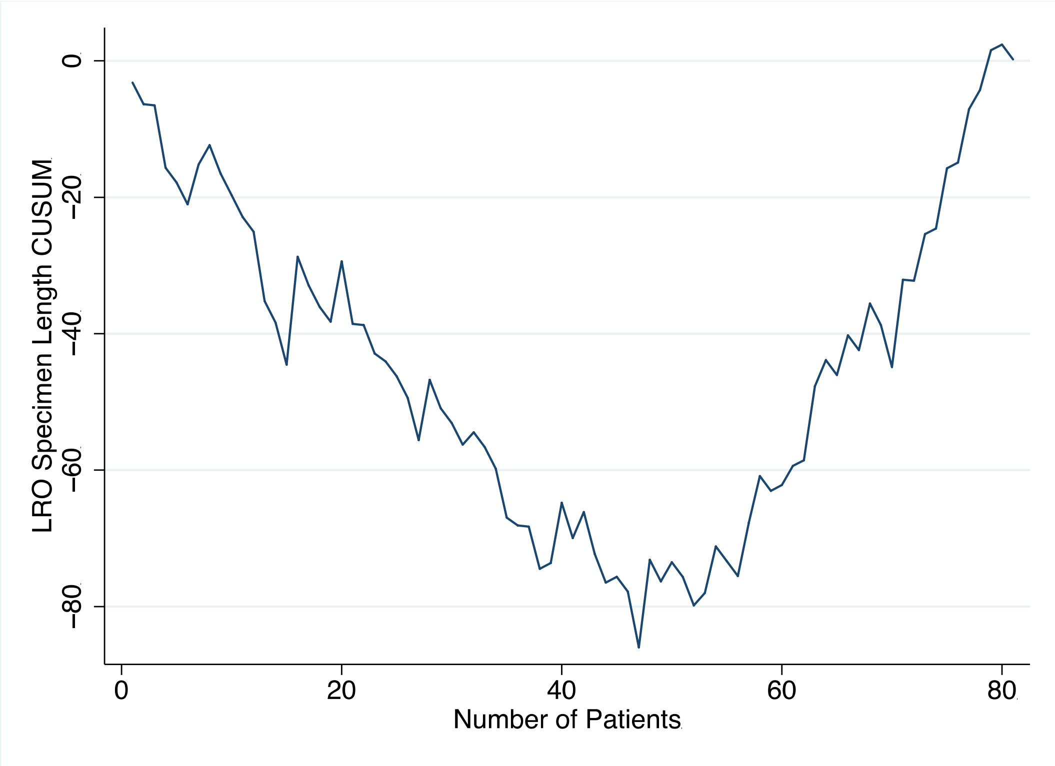

Figure 15. LRO specimen length CUSUM analysis

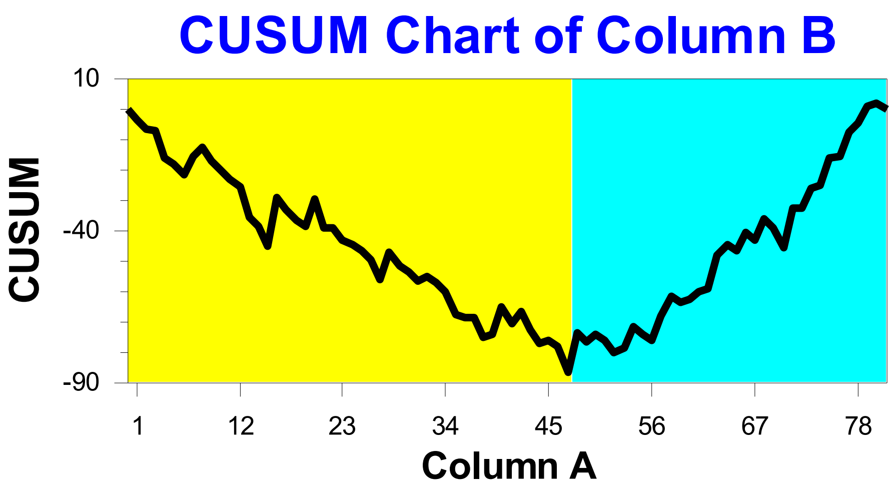

Figure 16. LRO specimen length CPA analysis

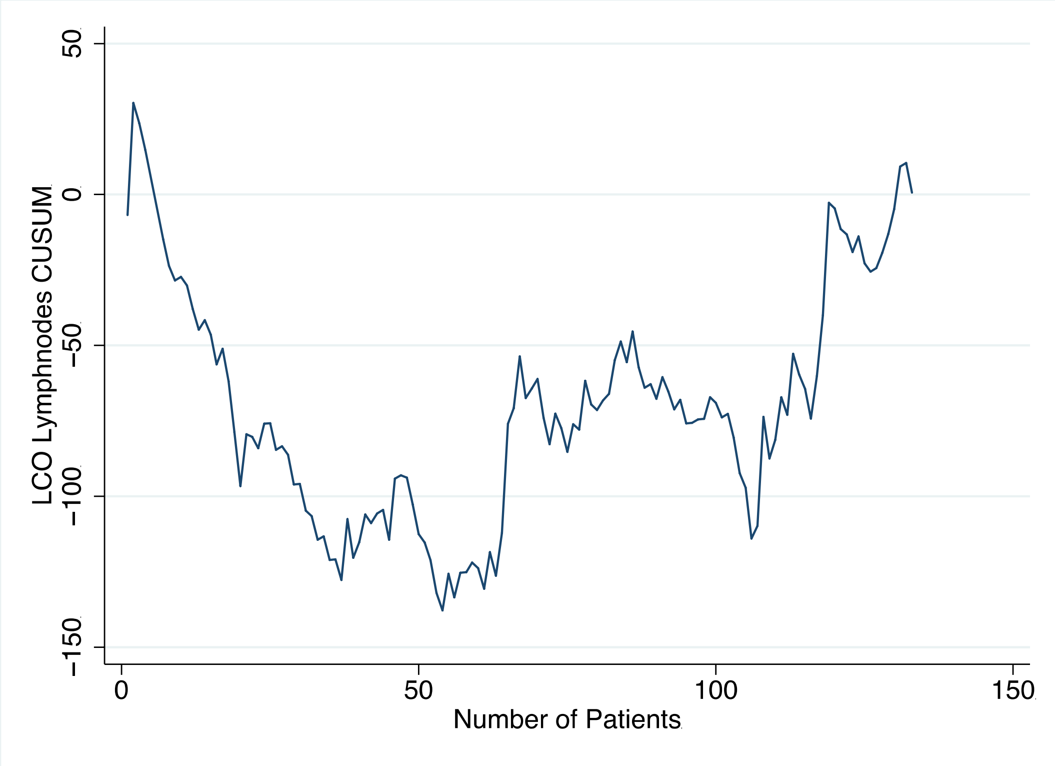

Figure 17. LCO lymph-nodes CUSUM analysis

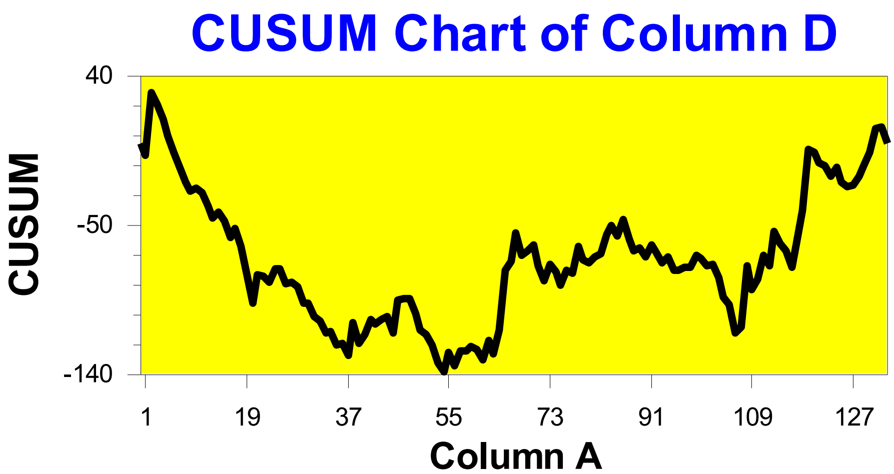

Figure 18. LCO lymph-nodes CPA analysis

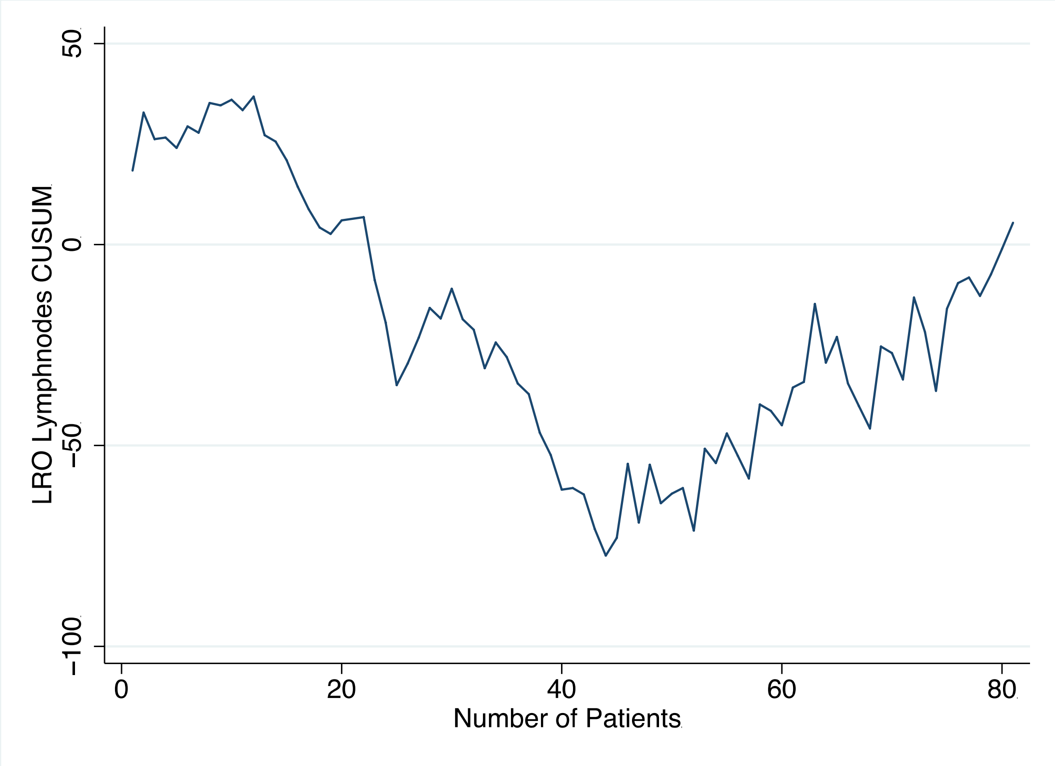

Figure 19. LRO lymph-nodes CUSUM analysis

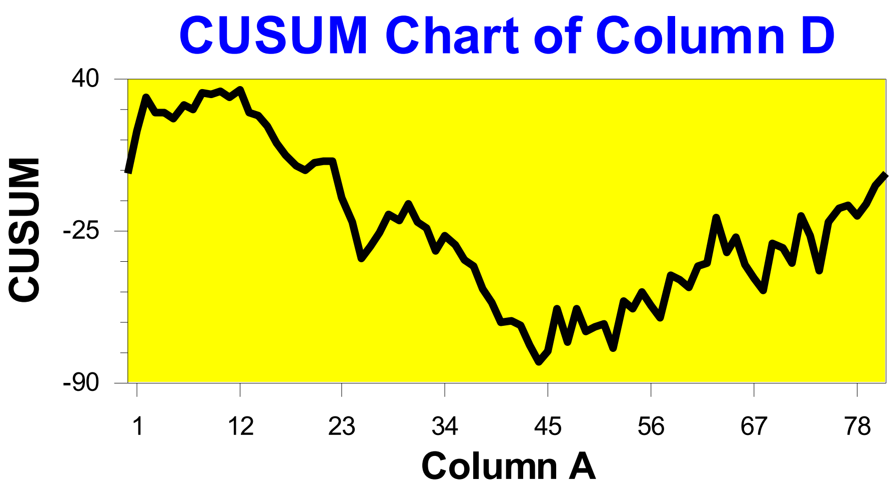

Figure 20. LCR lymph-nodes CPA analysis