LEARNING CURVES IN MINIMALLY INVASIVE THORACIC SURGERY.

by

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CHAPTER I

SYSTEMATIC REVIEW OF LEARNING CURVE METHODS IN MINIMALLY INVASIVE THORACIC SURGERY

ABSTRACT

Introduction: As the number of minimally invasive technologies increases in the field of thoracic surgery, so have the number of learning curve analyses performed for these innovations. Variation in learning curve methodology makes between-study comparisons and evidence syntheses difficult. Furthermore, poorly described and reported learning curve analyses make the results difficult to apply to different clinical settings. The objective of this systematic review is to characterize the variability in the methods used to construct and describe learning curves, with the goal of identifying shortcomings and potential areas for improvement in this line of research.

Methods: A search of Ovid Medline, Ovid Embase, EBSCO CINAHL, and Web of Science was performed. Studies of learning curves of anatomical lung resection operations in adult patients published in the English language were eligible for inclusion. Two reviewers independently assessed studies for eligibility, and extracted relevant data.

Results: The search yielded 56 articles eligible for inclusion in the present review. A variety of methods were used to construct the learning curve, with chronological grouping of cases being the most commonly used technique in 22 (39.29%) studies, followed by the cumulative sum method, employed in 21 (37.50%) studies. A total of 15 unique metrics were used for learning curve analyses; operative time was the most common metric, used in 39 (69.64%) studies. A large proportion of studies failed to provide details on learning curve parameters such as competency thresholds, surgeon's prior experience, case complexity, and learning curve definition. Considerable heterogeneity was found in the methods and reporting standards of learning curve evaluations in minimally invasive thoracic surgery.

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INTRODUCTION

Minimally Invasive Surgery

Minimally invasive surgery is a branch of surgery that involves the coordinated use of flexible cameras and mechanical instruments inserted through small incisions made in the thoracic cavity or other organ spaces to perform surgical procedures.[1] Tiny instruments are manipulated by the surgeon and assisting staff based on information that is relayed through a fiberoptic camera and displayed by high-definition monitors that facilitate real-time viewing and navigation of the surgical field.[2] Minimally invasive techniques in thoracic surgery have risen to prominence in recent years, nearly replacing open approaches for many procedures. Minimally invasive thoracic surgery entails two main approaches: video-assisted and robot-assisted thoracoscopic surgery.[3] In video-assisted surgery, a thoracoscopic camera and instruments are inserted into 1-2cm intercostal incisions. These instruments are used for a variety of functions such as cauterization, visualization, mobilization, stapling, and cutting to facilitate surgical procedures.[4] Robotic surgery, a more recent minimally invasive innovation, implements similar instrumentation through physician-guided movements that are executed by a robot at the patient's bed-side.[5]

Minimally Invasive Thoracic Surgery

The field of thoracic surgery has seen a rising trend in the number of cases performed through minimally invasive approaches.[5] Well established minimally invasive surgical procedures, such as video-assisted thoracoscopic surgery have demonstrated oncologic safety and efficacy in the field of thoracic surgery. Evidence now lends support to thoracoscopic techniques leading to reduced length of stay,[6] decreased blood loss,[7] improved pain control,[8,9] and oncologic efficacy,[10] notwithstanding improved cosmesis conferred by smaller "keyhole" incisions. Furthermore, techniques using the robotic surgical platform such as robot-assisted thoracoscopic surgery have additional benefits in the context of lung and mediastinal procedures. While obtaining similar outcomes to VATS,[11] robotic procedures provide enhanced three-dimensional visibility, namely for mediastinal procedures,[12] improved ergonomics for surgeons, increased lymph node clearance,[13] and increased degrees of freedom of the wrist during operations.[14]

With the increasing penetrance of minimally invasive technologies in the operating room, issues pertaining to skill acquisition and surgeon education become relevant. Despite pronounced advantages, the uptake of minimally invasive surgical procedures and concurrent medical curricula are lagging.[15-17] High operational costs,[18] potentially longer operative times,[19] resource intensive processes associated with trainee mentorship,[20] and a scarcity of robotic surgical devices in medical programmes[21] serve as barriers to adoption of robotic technologies. In addition, many surgeons who prefer VATS or open procedures express reluctance in adopting robotic techniques.[22] Thus, the ability to adopt new and cutting-edge technology may be challenging for minimally invasive thoracic surgeons and medical trainees.

Surgical Learning Curves

The finding that some minimally invasive procedures result in longer operative times is thought to be in large part due to the presence of a learning curve—the period in which surgeons are performing at a suboptimal level due to procedure novelty and relative inexperience in the technique under study.[5,22-24] Thus, physician education and the ability to perform a procedure competently are important considerations when making decisions at the patient, physician, and hospital administrator level. New technologies should strike a balance between potential benefits accrued to patients and providers, as well as a manageable learning curve that does not put patients at undue risk during the skill acquisition period. From a cost-utility perspective, incremental improvements in health status afforded to patients by the acquisition of new technologies reach an asymptote, whereas costs continue to rise, and the need to optimize quality of care becomes paramount.[25] Therefore, the evaluation and reporting of the learning curve in minimally invasive thoracic surgery, when studied accurately and objectively, can provide unique insight into the utility of procedures being considered for adoption.

Learning curves were first described in the aircraft industry, where they were initially used to model the number of man-hours needed to produce a single aircraft unit.[26] Since this time, the learning curve has been translated from measuring changes in industrial processes into a number of other contexts and has since become a practical tool for monitoring healthcare processes.[27] In the field of surgery, the learning curve characterizes the trajectory of learning, or learning-course, of a new procedure over a period of time. Typically, surgeon performance is determined using a surrogate measure, such as a process variable (i.e. operative time), and variations are observed over a consecutive number of cases. The archetypal learning curve includes an initial period of difficulty followed by a period of improvement, after which point surgeon performance experiences little change and reaches a point of stability. It is important to note that reaching a plateau in the learning curve does not necessarily indicate attainment of skill or proficiency, only that the operator demonstrates little to no further improvements.[28] Interest in characterizing the learning curves for different surgical procedures has risen in recent years due to its ability to derive useful information pertaining to surgical quality, patient outcomes, physician credentialing, and associated costs and benefits of surgical procedures.

Issues of Learning Curve Evaluation in Minimally Invasive Thoracic Surgery

Unfortunately, with the increased study of surgical learning curves came increased heterogeneity in the methodologies used to characterize them. This heterogeneity in learning curve methodology has been well characterized in the surgical literature in areas such as minimally invasive abdominal surgery[29] and robotic surgery.[30] Harrysson et al.[29] and Kassite et al.[30] report substantial heterogeneity in the types of outcomes used in learning curve studies, as well as in the statistical strategies and visual depictions used to construct the learning curves. This variation in methods between individual studies makes it difficult to compare the learning curves of different surgical procedures, which is important for guiding decisions related to physician education and the procurement of new surgical technologies. Furthermore, poor descriptions of learning curve analyses may also limit the interpretability and applicability of results, making it difficult to apply the results to a surgeon's personal practice.

Thoracic surgery is an evolving field in which new skills and procedures are continually required and employed. While a recent systematic review by Power et al.[31] describes the learning curves in studies of major robotic lung and mediastinal resections, the methods used to characterize these learning curves have yet to be explored. Despite this investigation, the previously described heterogeneity precludes the ability to perform between-study comparisons and/or pooling of data to estimate an average learning curve of a given minimally invasive thoracic surgical procedure. Therefore, this systematic review was conducted to determine the methodological quality of the learning curve literature in minimally invasive thoracic surgery.

Study Aims

The objective of this systematic review is to determine how learning curves are assessed in the thoracic surgical literature by collecting data on the outcomes and definitions employed, as well as the resulting learning curves generated for video and robot-assisted thoracic lung resections. Information from this review will help inform the following section of this thesis by identifying current trends in the physician education literature as it pertains to surgical learning curves. Therefore, the primary purpose of this review is to critically assess the study designs used to evaluate learning curves in minimally invasive thoracic surgery, characterize the variables and methods used to measure and analyze these learning curves, as well as how learning curves are portrayed and graphed.

METHODS

This systematic review is reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[32] The PRISMA checklist is presented in (Appendix 1). The protocol for this review will be made available upon request. This review is not registered as it did not meet the eligibility criteria for registration in the PROSPERO database.

Search Strategy

The search strategy was designed to comprehensively capture studies assessing learning curves of minimally invasive thoracic surgical procedures involving anatomical lung resection. A literature search was conducted on November 9th, 2020, using four electronic databases: Ovid Medline (1946 to November 2021), Ovid Embase (1974 to November 2021), EBSCO CINAHL (1961 to November 2021), and Web of Science (1900 to November 2021). Studies published in the English language were eligible for inclusion in this review. No other restrictions, date or otherwise, were imposed on the database searches. The search strategy was created with the assistance of a health sciences librarian (JP), and is presented in Appendix 2 and was informed by terms used to index relevant and recently published studies on the subject of this review. Titles, abstracts, and full-texts of relevant trials were also assessed for pertinent search terms related to the controlled vocabulary and keywords search concepts.

Study Eligibility

Studies of anatomical segmental resection, lobectomy, pneumonectomy, wedge resection, and combinations of various lung resections (removal of multiple segments or lobes e.g.

bilobectomy) in adult patients (aged 18 years or older) were eligible for inclusion. In order to be considered a minimally invasive procedure, the surgical approach must have involved thoracoscopic port insertion via video- or robot-assisted surgery. Studies of other thoracic procedures, including lymphadenectomy, thymectomy or esophagectomy, treatment of spontaneous pneumothorax, as well as routine non-therapeutic surgical procedures, such as exploratory thoracotomy or laparotomy, endoscopy, bronchoscopy, or organ biopsy were considered out-of-scope for the current review and were therefore not included. Studies evaluating the learning curve for cardiac surgical procedures were also ineligible for inclusion. Cardio-thoracic studies that reported on a subset of thoracic surgical patients were included so long as other inclusion criteria were met. Studies were eligible for inclusion regardless of the number of surgeons, or surgeries performed.

To be eligible for inclusion, articles must have addressed the learning curve and formally analyzed it by any kind of graph, table, or statistical technique. Study designs eligible for inclusion were prospective and retrospective cohort studies, case-series, as well as trials with or without a comparator arm. Individual case studies, review articles, letters, and comments were not eligible. In cases where the results of the trial were presented in both abstract and full-text publication form, the full-text publication was preferentially included and used for data extraction. Studies that have been published as a conference abstract with no accompanying full-text publication were excluded. Studies that were descriptive in nature, or evaluated the learning curve of a simulated procedure, as well as animal model studies were ineligible for inclusion in this review.

Study Selection

All articles retrieved from the database search were screened for inclusion eligibility. First, two reviewers (PRAM and NM) independently screened a pilot sample of 50 articles for potential relevance based on title and abstracts. This was done to ensure inclusion/exclusion criteria were applied correctly. After consolidating results from the first 50 articles, the two reviewers proceeded to screen the rest of the articles in a similar manner. Those publications identified to be potentially relevant underwent a second round of screening by the same two independent reviewers, who reviewed the full text of these articles to ensure all inclusion criteria were met. Both rounds of screening ended with a meeting between the two reviewers to consolidate inclusion/exclusion decisions. Disagreements were resolved through discussion and arbitrated by the senior author (WCH) if consensus was not reached.

Data Extraction

The main focus of this review was to collect information regarding the learning curve, how it was defined, and assessed in the methods section of the studies captured from the search strategy. A data extraction form was designed *a priori,* and the following information about each included study was extracted, in duplicate: study population, study design, study intervention, learning curve parameters and learning curve results. Information on the following learning curve parameters was collected: [1] Learning curve outcomes used (and explicit use of definitions), [2] inclusion and description of surgeon's previous experience, [3] inclusion and description of a pre-defined competency threshold, [4] control for confounding, [5] number of cases required to overcome the learning curve, [6] and visual depiction of the learning curve. These parameters have previously been found to be inconsistently, or under-reported in similar systematic reviews in other surgical specialties.[28] For studies that included a CUSUM analysis, information on the type of CUSUM chart used, details regarding the parameters used to construct the chart, case-mix adjustment, and interpretation of graphs to the reader, was also collected. Other information regarding the learning curve, such as the number of phases of the curve, and whether the learning curve was overcome, was also collected.

Data were extracted independently, in duplicate by two reviewers (PRAM and NM), and results were consolidated. Since the primary focus of this review was to describe the way that the learning curve has been reported in the literature, no quality assessment of the included articles was performed. Data was stored in an electronic data collection form (Microsoft Excel 365, 2021, Redmond, WA, USA).

Dealing with Missing Data

Data abstraction from full-text articles was completed for all included studies. In the case that data was not made available in the full-text, an attempt was made to retrieve missing data by contacting corresponding authors with request for further information (i.e. unpublished results).

Risk of Bias in Individual Studies

Since this review is concerned with the methods used to assess the learning curve, rather than the results obtained from the learning curve analyses, risk of bias was not assessed.

Synthesis of Results

We performed descriptive statistics to summarize the information collected from the included studies. Learning curve outcomes were classified according to the Donabedian Quality of Care model. Outcomes that overlapped multiple domains, or that combined multiple outcomes into a single measure (i.e. surgical failure), were classified as "composite" outcomes. Due to the nature of this review, and in line with the purpose of characterizing the methods used to study surgical learning curves in thoracic surgery, a meta-analysis was not performed. All statistical analyses were performed using IBM® SPSS® Statistics software (version 21.0) and all graphs were generated using SPSS® and Tableau Desktop (version 2021.1) on mac.

Donabedian Classification

The Donabedian Quality of Care model, originally described by Dr. Avedis Donabedian in 1966 is a conceptual framework used to measure quality of care in healthcare settings.[33] The model, depicted as a target, places the performance of physicians and other related healthcare practitioners as the "bull's-eye", with different factors, such as setting, patient adherence, and level of familial/community support, influencing the quality of healthcare, encircling the target (Appendix 3). These integrative elements of quality assessment are further characterized into three disparate yet connected domains: "structure", "process", and "outcome".[25] Structure refers to capital, both human and material, as well as the organizational setting in which care is sought. Process refers to the provision of healthcare and the processes involved in diagnoses and treatment. Outcome refers to any change in health status of patients and populations by the way of effective care. The Donabedian framework has been widely implemented and validated in a number of healthcare contexts, including cardiac,[34] emergency,[35] and rectal surgery.[36]

RESULTS

Search Results

The electronic database search yielded a total of 1614 articles. After the title/abstract and full-text review screening phases, 56 articles remained eligible for inclusion in the present systematic review[37-92]. The PRISMA flow chart is presented in Appendix 4.

Characteristics of included studies

Characteristics of the included studies are presented in Table 1 and Appendix 5. The final sample of included articles consisted of 50 retrospective and prospective cohort studies and 6 consecutive case-series. The included studies were published between the years 1993-2020, however the vast majority of studies (39/56; 69.64%) were published from 2016 onward (Table 1 and Appendix 6). Learning curve studies in thoracic minimally invasive surgery were mostly performed in Asia (23/56; 41.07%), followed by Europe (16/56; 28.57), and North America (12/56; 21.43%). Video-assisted surgery was the most common surgical approach, used in over half (38/56; 67.86%) of the included studies, followed by robot-assisted surgery in 17 (30.36%) of the studies. Only one study (1.79%) evaluated the learning curve of both video- and robot-assisted thoracic surgery. Lobectomies were the most commonly performed surgeries, followed by segmentectomy, in 37 (66.07%) and 8 (14.29%) of included studies, respectively.

Table 1. Characteristics of Included Studies	
N=56 studies, unless otherwise stated	Total
<u>Sample Size</u>	
Number of participants per study, n (%)	
1-50 patients	4 (7.14)
50-100 patients	15 (26.79)
100-250 patients	21 (37.50)
>250 patients	16 (28.57)
<u>Study Information</u>	
Total patients included, n	41,060
Year of publication, median (25-75%)	2017 (2011-2020)
Study Location, (%)	
Asia	23 (41.07)
Europe	16 (28.57)
North America	12 (21.43)
South America	2 (3.57)
Multiple	3 (5.36)
<u>Surgeons</u>	
Number of surgeon(s) per study, n (%)	
1	28 (50.00)
1-5	11 (19.64)
≥5	4 (7.14)
Non-Specified	13 (23.21)
Previous Training Reported, n (%)	38 (67.86)
Type of previous training, n (%); N=38	
Video-Assisted	17 (44.74)
Open	4 (10.53)
Mixed	12 (31.58)
Technique not specified	5 (13.16)
<u>Surgery</u>	
Approach, n (%)	
Robot-Assisted	17 (30.36)
Video-Assisted	27 (48.21)
Uniportal Video-Assisted	11 (19.64)
Robot/Video-Assisted	1 (1.79)
Type of operation, n (%)	
Lobectomy/Bilobectomy	37 (66.07)
Segmentectomy/Subsegmentectomy	8 (14.29)
Multiple/Pneumonectomy	11 (19.64)

Learning Curve Characterization

Learning Curve Methods

Complete results of the methods used to characterize the learning curve are provided in Table 2. The most common method used to construct the learning curve was chronological grouping of cases (split-group analysis), which was performed in 22 (39.29%) studies. This approach involves dividing consecutive surgical cases into two or more groups (i.e. early and late phase, tertiles, etc.), and comparing outcomes between these groupings. The cumulative sum (CUSUM) method was the second most commonly used approach, used in 21 (37.50%) studies. A total of 6 (10.71%) studies reported using methods to control for confounding variables, including imputation, stratification, and risk-adjustment through logistic regression modelling.

Competency thresholds were reported in 35 (62.5%) studies and were most commonly used in CUSUM learning curve evaluations. The most frequent method to construct competency thresholds was through the identification of the inflection point or plateau on the CUSUM curve (21/35; 60.00%). Control limits and using a pre-defined number of cases were each used in 6/35; (17.14%) of studies that included a competency threshold. Significant improvement in measured outcomes was used as competency threshold in the remaining 2/35 (5.7%) studies.

While 21 (37.50%) studies exclusively used chronological grouping as the method to construct the learning curve, an additional 24 (42.86%) studies used a combination of chronological grouping and another statistical technique to evaluate the learning curve. For example, many studies (16/56, 28.57%) used the CUSUM method to construct the learning curve, and then divided the curve into phases to compare outcomes between the different phases in the learning process. In these cases, the different phases of the learning curve were identified using one of the aforementioned competency threshold techniques. The median number of learning curve phases was 2 (Interquartile Range (IQR), 2-3). Of these 45 studies, 43 (95.56%) used some form of parametric or non-parametric statistical test to assess differences between these groupings. Table 2 summarizes the number of divisions used in chronological groupings of the learning curves by frequency.

Table 2. Learning Curve Study Methodology

N=56 studies, unless otherwise stated

Study Methodology	Total
Learning curve method, n (%)	
Chronological Grouping only	22 (39.29)
CUSUM + Chronological Grouping	16 (28.57)
Regression	7 (12.50)
CUSUM only	5 (8.93)
Weighted Average	2 (3.57)
Other	4 (7.14)
Competency Threshold Type, n (%); N=35	
Plateau/Inflection Point	21 (60.00)
Control Limit	6 (17.14)
Pre-defined Number of Cases	6 (17.14)
Significant Improvement in Outcome	2 (5.71)
Graphical Representation, n (%); N=46	
Line/Bar/Scatter/Box plot	16 (34.78)
CUSUM curve	16 (34.78)
Regression	4 (8.70)
Kaplan-Meier Curve	3 (6.52)
Receiver-Operating Curve	1 (2.17)
Multiple	6 (13.04)
Control for Confounding, n (%); N=6	
Risk-adjusted model	4 (66.70)
Stratification	1 (16.70)
Imputation	1 (16.70)
Split-group Analysis	
Number of studies split into phases, n (%)	45 (80.36)
Number of phases, n (%); N=45	
2 phases	24 (53.33)
3 phases	14 (31.11)
4 phases	5 (11.11)
5 phases	2 (4.44)

Abbreviations: CUSUM, cumulative sum.

Learning Curve Outcomes

Across the 56 included studies, a total of 15 unique outcomes were used for the learning curve analyses. The median number of learning curve outcomes used in the included studies was 1 (IQR, 1-2) (Appendix 7). The most commonly used learning curve outcome was operative time, which was used in 39 (69.64%) of the included studies. The remaining outcomes were much less frequently reported, each appearing in <10 studies. Six (10.71%) studies reported at least one composite outcome, comprised of two or more individual endpoints combined into a single outcome. The frequency of different parameters and variable domain as classified according to the Donabedian model is presented in Tables 3, Figure 1, and Figure 2. Process outcomes, such as operative time and conversions, were the most common type of variable domain reported in the included articles, appearing in 21 (37.50%) studies. Of note, there were no studies that included a parameter from the "structure" domain of the Donabedian model. In 12 (21.43%) studies, a primary outcome for the learning curve analysis was not specified. Of the 44 (78.57%) studies reporting a learning curve parameter, only 18 (32.14%) explicitly defined the variable used for analyzing the learning curve.

Table 3. Outcomes used to evaluate the Learning Curve

N=56 studies, unless otherwise specified

Outcome Reporting	Total
Outcome Frequency, n (%)	
1 outcome	19 (33.93)
2 outcomes	13 (23.21)
≥ 3 outcomes	12 (21.43)
Not Specified	12 (21.43)
Composite outcome, n (%)	6.0 (10.71)
Outcome Type, n (%)	
Structure	0 (0.00)
Process	21 (37.50)
Clinical Outcome	3 (5.36)
Process and Clinical Outcome	20 (35.71)
Unspecified	12 (21.43)

Figure 1. Outcomes used for Assessing Learning Curves in the Included Studies

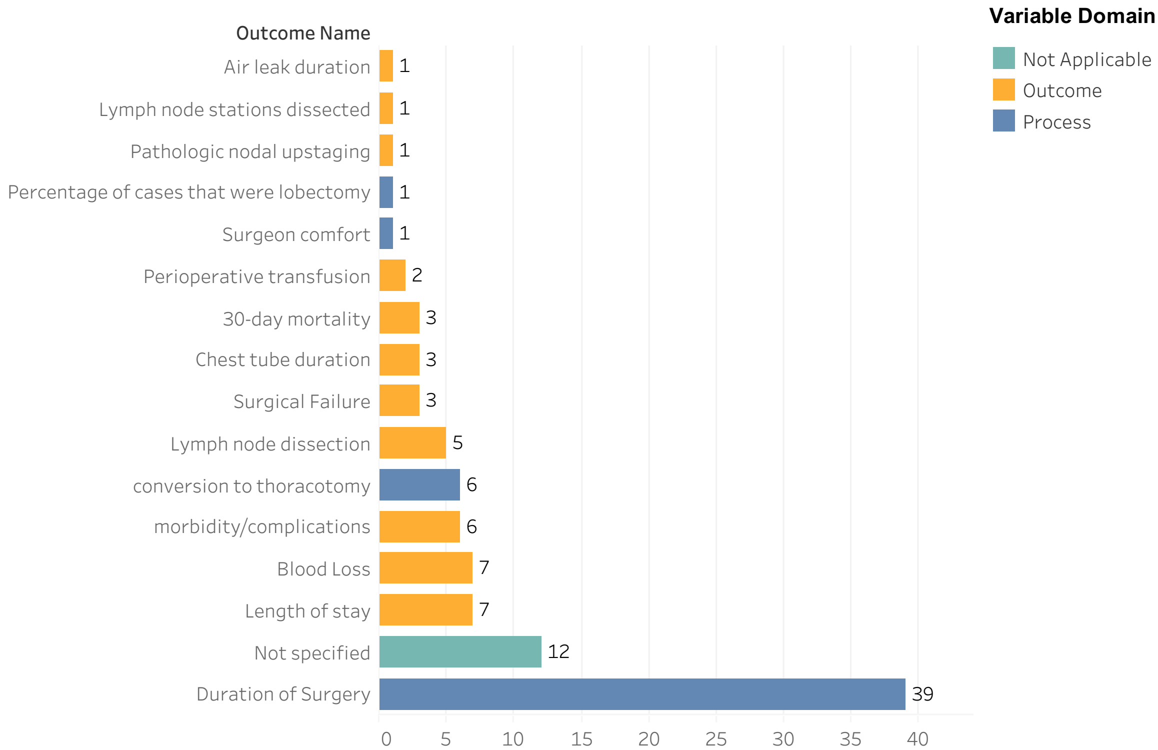
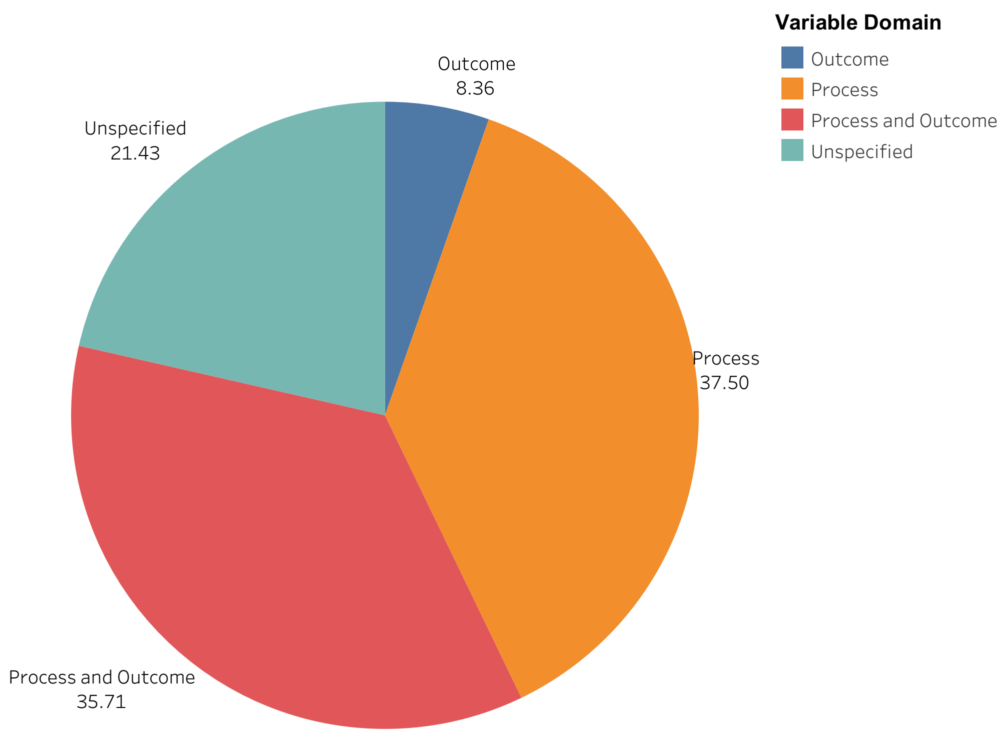


Figure 2. Distribution of Variable Domains used to Measure the Learning Curve Categorized by the Donabedian Model



Standards of Reporting

Amongst the 56 studies included in this review, the learning curve was reported to be overcome by 46 (82.14%) of the included studies, despite only 35 studies (62.5%) setting a predefined threshold to signify when the surgeon reached competency, with approximately one-third (12/35, 34.28%) of studies providing some form of justification for the chosen threshold value. A definition of what constituted the learning curve was provided for 33 (58.93%) studies. The majority of studies (38/56, 67.86%) provided some description of the surgeon's prior training and experience. A description of the patient case-mix was also provided in most studies (50/56, 89.29%), however only 7 studies (12.50%) included a gradation of case complexity.

Across the included studies, 10 unique methods were used to graphically represent the learning curve. A CUSUM graph was the most commonly used graphical depiction in 19 (33.93%) studies, followed by a scatter plot, used in 17 (30.36%) studies. Ten (17.86%) studies provided only a tabular or textual description of the learning curve without any visual depiction. Table 4 summarizes the various types of graphs used to visually depict the learning curve, and the frequency with which they are used in the included studies.

Table 4. Graphical Representations of Learning Curves

Graphical Representation	**Number of Studies***
CUSUM	19
Scatter Plot	17
Regression	5
Kaplan-Meir Curve	3
Line Graph	2
Bar chart	1
Box-Plot	1
Cubic Spline	1
Receiver Operating Curve	1
LOWESS (time-series analysis)	2

*Some studies presented more than one graphical representation of the learning curve. 10 studies provided only a tabular or textual description of the learning curve. CUSUM, cumulative sum; LOWESS, locally weighted scatter plot smoothing.

DISCUSSION

This review identifies substantial heterogeneity in the metrics, methods, and standards of reporting across 56 studies that assessed the learning curve in minimally invasive thoracic surgery. In addition, our review indicates variation in the definitions and endpoints used to assess the learning curve. Heterogeneity outlined in this review highlights the ongoing challenge of limited interpretability of the increasing number of learning curve studies published in the minimally invasive thoracic surgical literature, a trend that has been paralleled in other surgical disciplines.[28,93]

One of the most striking findings from this review is the variability in the way learning curves are constructed, defined, and evaluated. The majority of studies comprising this review used either chronological grouping (22/56; 39.29%), a variation of the cumulative sum method (5/56; 8.93%), or a combination of these two learning curve methods (16/56; 28.57%) to construct and evaluate the learning curve. CUSUM is a quality control charting method used to measure cumulative deviations of observations from a pre-specified value (often based on the mean value of the dataset or a historical standard) and is sensitive to sustained degradation of surgical processes.[8] Initially used for maintaining quality control over industrial processes,[94] CUSUM methodology has been adopted by clinicians to study the surgical learning curve in many disciplines, namely cardiothoracic procedures.[95,96] Researchers have taken many different approaches to summarizing and describing CUSUM methodologies.[97-99] Despite these efforts, there remains much debate and contention regarding the optimal use of CUSUM.[100] Appropriate use of control limits,[101] inclusion of adjustments for case-mix and complexity,[95] and prospective versus retrospective application of process monitoring,[102] are all areas of active CUSUM methods research.

Competency thresholds, (often referred to as control or decision limits in quality control chart methodology) are important components of chart construction and represent pre-defined limits of performance used to monitor whether a process is “in” or “out” of control.[103] When a threshold boundary is crossed in a learning curve analysis, sufficient progress has accumulated to signal that competency has been reached. In the present review, over half of studies (35/56; 62.50%) included a competency threshold used to measure the learning curve, however, there was a lack of consistency in the way thresholds were determined amongst those that had reported one. There exists considerable debate in the literature for the best way to construct these limits, and methods are dependent on the type of control chart monitoring applied.[97] Many studies (21/35; 60.00%) characterized the learning curve by when a surgeon reaches a plateau in performance[43,48,52,55,56,60,61,67,70,73,74,79,80,83,86,90] or when a point of inflection is reached in the curve.[40,44,59,69,75] While this approach indicates a point at which competence remains stable, it does not necessarily indicate that the learning curve has been overcome. In addition, the number of cases before plateau may differ from one surgeon to the next, and depending on the outcomes used to measure the learning curve, this may be a poor indicator of overall surgical quality. For example, multiple studies identified inflection points in the learning curve without corresponding improvements in clinical outcomes.[40,56] Furthermore, the identification of a plateau can be subjective and is often identified using crude methods such as visual fit alone. Indeed, unless the sample size is sufficiently large, a plateau in the learning curve may never be reached. Other methods involve using reference values from the literature, the average value of the dataset, or the number of procedures to achieve a threshold set by experienced surgeons. Not only do these methods require familiarity with quality control monitoring techniques, which may not be immediately available to clinicians or administrators who would benefit from the information from these types of studies, but implementing learning curve thresholds in any of these ways may also lead to oversimplification or overinterpretation of the learning curve, thus contributing to the difficulty of evaluating learning curve data. Woodall et al. have critiqued the use of CUSUMs that accumulate successive differences between the performance metric values and their average, since they are invariant to the addition of a constant to the time series values.[102] For example, a CUSUM curve measuring operative time with the following series data 175, 145, 165, 135 when compared with another data series 195, 165, 185, 155 would be represented by identically shaped curves, despite differing levels of performance. Therefore, expert consultation is required in the interpretation of the learning curve data when interpreted in this way.

Furthermore, many studies concluded that the learning curve was overcome, despite lacking a defined competency threshold,[68,72,85,87] and in select instances, without defining what the learning curve represented.[39,46,62,63,65,76,78,82,84] In contrast, many studies failed to explicitly state whether the learning curve had or had not been overcome,[41,49,51,54,58,64,81] even when a competency threshold had been defined by study authors.[50,60,92] Competency thresholds that are defined *a-priori* should be constructed with self-contained rationale provided by study investigators in order to allow for easier interpretation. For example, competency thresholds may reference an expert derived proficiency level, or based on decision limits that represent clinically significant deviations in performance cited in the pertinent literature. The strength of the provided justification should always be considered when interpreting the results of any learning curve evaluation.

Outcome selection is another challenge in the learning curve literature. One of the main drives for outcome selection in learning curve methodology is to provide a proxy of health care quality. Traditional CUSUM methods rely on binary outcome data use, however, contemporary

CUSUM approaches that use continuous time-based metrics have populated the surgical learning curve literature, refreshing the discussion of optimal outcome selection in these analyses. In this review, operative time was the most commonly reported outcome when assessing the learning curve (39/56; 69.64%), as is seen in systematic reviews conducted in other surgical contexts.[104] Reliance on the use of process outcomes such as operative time or conversion rate, suggests an underuse of the structure and outcome domains as outlined by the Donabedian model when monitoring and evaluating the surgical learning curve. In the present review, 41 studies (73.21%) reported at least one variable from the process domain, while just 23 studies (41.07%) reported a variable from the outcome domain, and none reported a variable from the structure domain. The frequency with which time-based variables are used in the learning curve literature is an interesting observation that warrants further exploration. Operative data is routinely collected, and its availability makes it a convenient target for primary outcome selection in learning curve studies. However, expediency alone does not ensure clinically relevant measures of learning.[105] Factors such as patient volume, case-mix and complexity, non-technical skills and team expertise are additional elements that impact the patient experience and are not adequately captured in the unidimensional analysis of operative time.[106] Though it may provide useful information regarding a single surgeon/operator, in isolation of other factors, it is not an appropriate surrogate of overall surgical quality. On the contrary, outcomes such as operative mortality may not be relevant for the evaluation of low-risk procedures. Therefore, in selecting an outcome variable for the learning curve analysis, a multi-variable approach incorporating patient-important outcomes tailored to the operation under study should be considered when planning learning curve investigations or surgical procedures. The Donabedian model (Appendix 3) provides a useful conceptualization of outcomes under “process”, “structure”, and “outcome” domains, which can be used when planning learning curve analyses.

This review reveals a broad range of variables used to measure the learning curve; a total of 15 unique outcomes were used. Variation exists not only in the variables selected to define the learning curve, but in the definition of those variables as well. Many studies failed to explicitly define the outcome under study. For example, many studies that used time-based metrics did not provide a definition for the parameters that constituted the duration of surgery, or did not distinguish between console, docking, or total operative time.[42,43,45,46,54,56,59,61,62,64,67,69,72,78,80,83,87] Use of explicit definitions becomes relevant when comparing learning curves between studies or when trying to contextualize the results to inform health related decision making. For example, Song et al. demonstrated differences in the learning curve for robot-assisted lobectomy depending on which of the aforementioned time-based parameters were implemented.[79] The use of composite outcomes in this review also highlights the difficulty of incorporating complex binary patient outcome variables when studying the learning curve. Surgical failure was included as a binary outcome to measure the learning curve in multiple studies in this review, though its definition was also variable.[44,89,90] In one study, surgical failure involved major perioperative morbidity and mortality, excessive blood loss, and extended duration of surgery greater than two standard deviations above departmental average,[89] however, in another study, only conversions, complications, and hospital readmissions constituted surgical failure.[90] Despite studying the same surgical technique and approach, these discrepancies again highlight challenges in the ability to compare learning curves.

This study also highlights deficiencies in learning curve standards of reporting. A large proportion of studies included in this review failed to report on important study characteristics for appropriate learning curve characterization, such as previous surgeon experience, identification and definition of primary outcome used for learning curve analysis, or justification for the use of a certain competency threshold. Taken together, greater detail and more transparent reporting of study characteristics in the thoracic surgical learning curve literature will allow for study results to be generalizable and reproducible.

In recent years, there has been an increase in the uptake of minimally invasive techniques in the field of thoracic surgery.[5] The increasing popularity of minimally invasive techniques can be attributed to their improved safety, less pain, and shorter hospital stays compared to the conventional open approaches, particularly in the context of complex cases.[3] As minimally invasive technologies continue to evolve, it is to be expected that in the coming years, more studies evaluating the learning curve of these procedures will be published. Indeed, this trend has already been observed in the present review (Appendix 6). With likely increases in time, effort, and resources that will be poured into conducting this type of research, it becomes imperative for the research community to standardize and optimize learning curve methodology in order to ensure these future learning curve studies are methodologically sound, and can be meaningfully used to guide decision-making by clinicians, administrators, and medical educators. The present review demonstrates a need for reporting guidelines to help ensure learning curves are well described and characterized, which will in turn improve the interpretability and application of results to other clinical contexts.

Kassite et al. echo similar suggestions in their review of learning curve studies in robot-assisted surgery, where they document significant range and heterogeneity across multiple surgical specialties.[107] They put forth recommendations for standardizing learning curve methodology by including the following components:

1. A direct indicator of success relevant to the procedure (oncological outcome for cancer surgery, functional outcomes for reconstructive surgery…);
2. AND a direct indicator of complications;
3. AND operative time (console time or specific procedural time).

The authors emphasize the use of CUSUM analysis, explicit definitions, and inclusion of controlling for as many confounders as possible. The author of the present review recommends the use of CUSUM quality control chart monitoring, with control limit implements based on acceptable and unacceptable performance values based on the available literature, wherever feasible. The construction of CUSUM curves with appropriate control limits have been outlined in a practical description by Rogers et al.[97] The present author also recommends operative time as a routinely collected measure of procedure efficiency, in conjunction with additional learning curve metrics of interest for the procedure under study. For example, operative time, in addition to resection margin status, may be outcomes of interest when studying sublobar resections in minimally invasive thoracic surgery. Subsequently, generated learning curves can be overlayed to analyze observable trends or deviations in performance. These recommendations are put forward in attempt to streamline the process of evaluation and interpretation of learning curves.

With the observed increase in surgical technologies and studies of their learning curves in recent years, it also becomes important to consider the unique ethical and legal ramifications of innovations in surgical practice. Operative outcomes and surgical quality of care provided cannot come at the expense of innovation. In the case of minimally invasive surgeries, procedure novelty can lead to several issues including increased potential for adverse outcomes, which may erode patient trust in their surgeon, create difficulty in fully disclosing procedure risks, and lead to inaccurate evaluation of patient outcomes due to lack of familiarity with the procedure.[108,109] Furthermore, unlike in resident training, where the procedures are well-understood and the attending physician and surgical team are able to assist, when dealing with novel procedures the surgeon and the surgical team have limited experience with the technique as well as the possible consequences, which strains the learning process.[110]

In order to ethically manage the issues arising from the surgical learning curve, it becomes imperative that the surgeon and surgical team uphold their moral obligation to prepare both technically and professionally. Technical preparation involves ensuring that one has the technical competency required to perform the novel procedure. This can be achieved through simulation exercises on cadavers or computers, which have also been the subject of learning curve studies,[111,112] shadowing experts and seeking their guidance, and sharing one's experiences and lessons learned with colleagues in the field.[110] The field of minimally invasive surgery has introduced new methods of training that minimizes the risks to patients. One of the most notable advantages is the ability to review surgical performances through intracorporal video feed and through dedicated simulation systems that are designed to mimic the operative experience. Compared to training in the operating room, video-based assessments do not require direct observation of performance, thus decreasing operating room pressures while allowing for blinded, unbiased assessment.[113] Additionally, video-based assessments can be paired with objective and validated rating scales, such as the thoracic competency assessment tool – anatomic resection for lung cancer (TCAR-ARC),[114] the global assessment tool for evaluation of intraoperative laparoscopic skills (GOALS)[115] or the global evaluative assessment of robotic skills (GEARS) to provide formative evaluations during attainment of surgical proficiency of a new procedure.[116] With the decrease in opportunities for real-time feedback in the operating room, and a renewed interest in patient safety initiatives, video-based assessment provides a safe and effective avenue to provide summative feedback for trainees or surgeons along the learning curve of a new procedure. The advent of minimally invasive technologies has also paved the way for telementorship initiatives that enables remote teaching without the burden of excessive travel or taking time off work to mentor.[117] In addition to becoming technically proficient during the adoption of a new procedure, surgeons should also prepare professionally by acting with integrity towards their patients and themselves.[110] This involves practices such as being transparent with patients about one's relative lack of experience, and evaluating and reflecting on one's experiences and outcomes with the procedure in question.[110]

To the author's knowledge, the present study is the first to characterize the methodologies and reporting standards of learning curve studies in minimally invasive thoracic surgery, being the first to characterize the methods used in the learning curves of both video- and robot- assisted procedures in the thoracic surgical specialty. As such, this review provides a comprehensive summary of the key strengths and shortcomings relevant to the study of learning curves in minimally invasive thoracic surgery, and serves as a starting point for future discussions on how best to optimize future research in this field to make it both methodologically sound, and relevant and useful to its end-users.

The present review has a few limitations. First, the full complement of learning curve studies in thoracic surgery is not captured in this review as conference abstracts were ineligible for inclusion. However, the decision to exclude conference abstracts from the present review was prompted by the severely limited information contained within an abstract, which would not allow for a fair appraisal of the methodology and reporting quality of the study. The results of this review may also be subject to publication bias resulting from unpublished work. To mitigate this problem, additional hand searches of the published literature were performed to identify other relevant studies. Field experts were not contacted to help identify other potential learning curve studies/research or unpublished data. Furthermore, a quality assessment of the studies was not performed since the purpose of this review was to characterize learning curve methodology, rather than to assess the reliability of the study results. However, such an assessment may have provided additional insight into the methodological quality of the included studies. Finally, a meta-analysis of individual study results was not performed as the included studies assessed a diverse range of surgical procedures that cannot simply be pooled and reduced into a single group without further standardization in the learning curve methodologies presented.

CONCLUSION

This systematic review explored the problem of heterogeneity in learning curve study methodology, which may preclude the pooling of results from individual studies into meta-analyses used to inform clinical practice. Variation in study methods makes comparisons of the learning curves between and within different surgical procedures difficult, and fails to optimize the full potential of learning curve analyses. Furthermore, poor descriptions of learning curve analyses may limit the interpretability and applicability of results. For example, if the pre-defined competency level is not defined in a study, or is set arbitrarily higher or lower than average, study results may not be useful to the average surgeon, who may find the results difficult to interpret and apply in his own clinical context. The increasing rate of minimally invasive surgeries suggests that the prevalence of learning curve studies will only see an increase in the future. Therefore, further development and investigation in the uptake of set reporting standards in learning curve methodology will allow for information generated from these studies to be used to inform medical curricula, physician education, and quality control monitoring processes.

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APPENDICES

Appendix 1. PRISMA Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	5
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	6
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	10
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	11
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	12,13
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	12
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	53
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	14,15
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	14
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	14,15
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	15
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	15
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	16
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	NA
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	15
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	16
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	16
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	NA
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	NA
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	NA
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	NA
RESULTS			

Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	17
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	17
Study characteristics	17	Cite each included study and present its characteristics.	56-66
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	NA
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	NA
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	NA
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	NA
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	NA
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	NA
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	NA
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	NA
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	17-23
	23b	Discuss any limitations of the evidence included in the review.	32,33
	23c	Discuss any limitations of the review processes used.	32,33
	23d	Discuss implications of the results for practice, policy, and future research.	30-33
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	12
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	12
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	NA
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	6
Competing interests	26	Declare any competing interests of review authors.	6
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	12

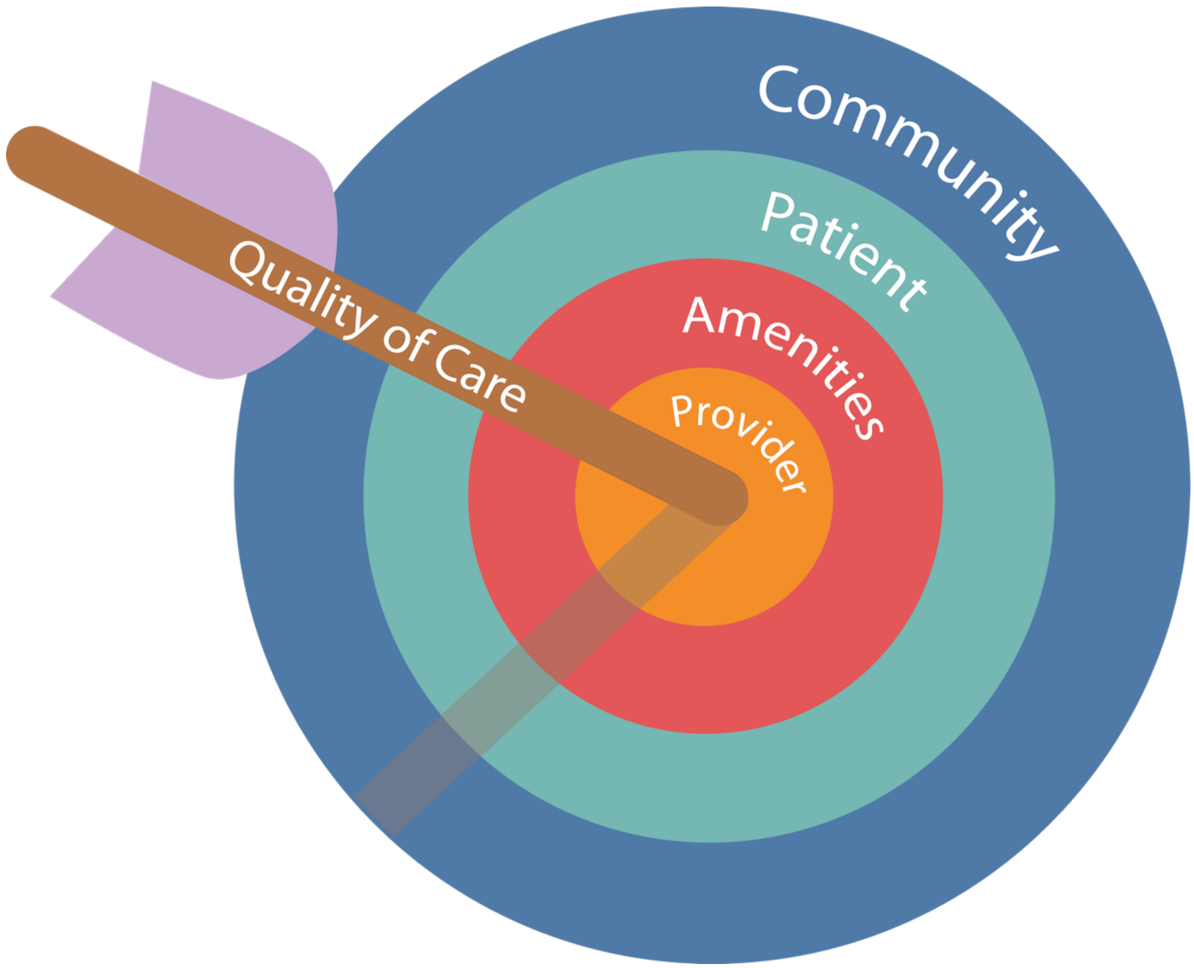
From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71

For more information, visit: http://www.prisma-statement.org/

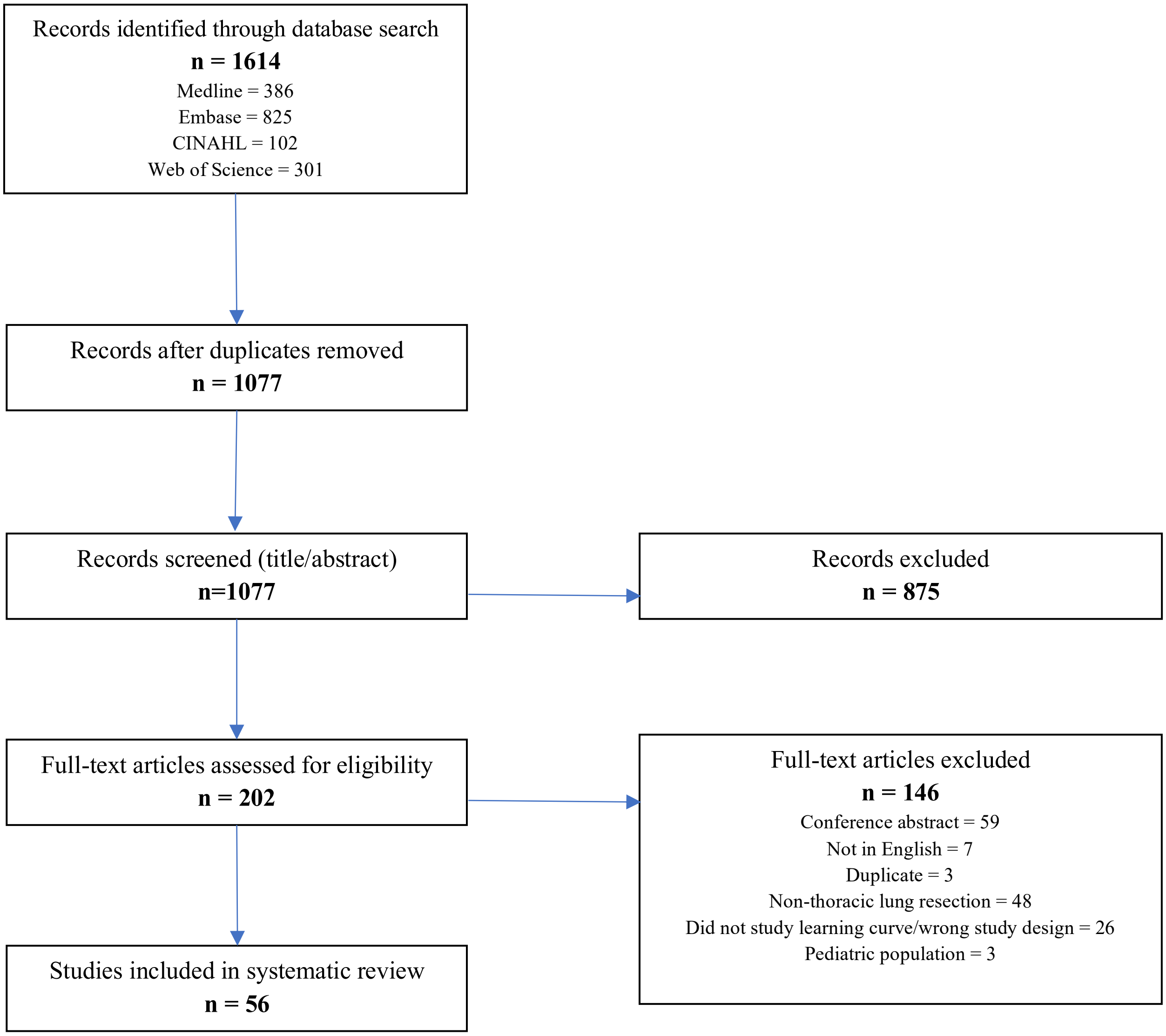
Appendix 2. Medline Search Strategy

1. ((lung OR pulmonary) adj2 (lobectomy* OR segmentectom* OR thymectom* OR resect* OR reduction OR excis*)).ti,ab,kw,kf.
2. (pneumoresection* or pneumectom* or pneumonectom*).ti,ab,kw,kf.
3. Thoracotomy/
4. Thoracotom*.mp.
5. (lung adj2 (reduction or resect* or excis*)).ti,ab,kw,kf.
6. Lung Disease*.mp.
7. Lung Neoplasms/
8. ((lung or pulmonary) adj2 (adenocarcinoma* or cancer* or neoplas* or tumo?r* or malignan* or carcinoma* or metas* or carcinogenesis or sarcoma*)).mp.
9. or/1-8
10. minimally invasive surgical procedures/ or thoracoscopy/
11. (minimally invasive surgical procedure* or thoracoscop* or video-assist* or uniport*).mp.
12. robotics/ or robotic surgical procedures/
13. robot*.mp.
14. or/10-13
15. 9 and 14
16. thoracic surgery, video-assisted/
17. (VATS or video assisted thora* or or video-assisted thora*).mp.
18. (video adj3 thora*).mp.
19. or/15-18
20. learning curve/
21. Learning curve*.mp.
22. Learning/
23. skill acquisition.mp.
24. Clinical Competence/
25. (clinical adj2 (skill* or competenc*)).mp.
26. "Outcome and Process Assessment, Health Care"/sn [Statistics & Numerical Data]
27. or/20-26
28. 19 and 27

Appendix 3. Donabedian Model: A Conceptual Framework of Healthcare Quality



Appendix 4. PRISMA Flow Diagram



Appendix 5. Summary of Included Studies

Author, Year	Patients	Sample Size	Surgical Approach	Type of Operation	Learning Curve Outcome	Number of Cases before Overcoming the Learning Curve
Muyun P et al., 2020[1]	Patients with benign and malignant lung lesions	153	Robot-assisted thoracoscopic surgery	Segmentectomy & Lobectomy	Operative time	20
Huang J et al., 2015[2]	Patients diagnosed with non-small cell lung cancer via bronchoscopy	13	Video-assisted thoracoscopic surgery	Double sleeve lobectomy with mediastinal lymphadenectomy	1. Operative time 2. Blood loss	Not specified
Feczko A et al., 2019[3]	Patients diagnosed with non-small cell lung cancer	4,483	Robot-assisted thoracoscopic surgery	Lobectomy	1. 30-day mortality 2. Perioperative transfusion 3. Major Morbidity 4. Operative time	de novo surgeons: 93 cases for 30-day mortality, 40 cases for major morbidity, 93 cases for perioperative transfusion, 40 cases for OR duration open-to-robotic surgeons: 95 cases for 30-day mortality, 67 cases for major morbidity, 90 cases for perioperative transfusion, 14 cases for OR duration video-assisted-to-robotic surgeons: 86 cases for 30-day mortality, 69 cases for major morbidity, 90 cases for perioperative transfusion, 21 cases for OR duration
Bedetti B et al., 2017[4]	Patients with primary lung carcinoma, metastatic disease, or infectious lung disease	73	Video-assisted thoracoscopic surgery	Uniportal lobectomy	1. Postoperative complications (air leak, pneumonia, aspiration and hypoxia) 2. Conversion to thoracotomy (non uniportal VATS) 3. Operative time	30
Amore D et al., 2018[5]	Patients with suspected lung cancer	573	Video-assisted thoracoscopic surgery	Lobectomy	Conversion	50

Taniguchi Y et al., 2017[6]	Patients with primary non-small cell lung cancer	44	Robot-assisted thoracoscopic surgery	Lobectomy & segmentectomy	Not specified	Not Specified
Yao F et al., 2017[7]	Patients with non-small cell lung cancer	67	Robot-assisted thoracoscopic surgery	Lobectomy	1. Operative time 2. Chest tube duration 3. Postoperative Hospital stay	26
Mazzella A et al., 2016[8]	Patients with lung cancer or non-infectious benign pathologies	119	Video-assisted thoracoscopic surgery	Lobectomy	1. Number of lymph nodes dissected 2. Operative time 3. Chest tube duration 4. Air leaks duration 5. Length of Hospital stay	30 for reproducibility, 90 before operative time decreased
Zhao H et al., 2010[9]	Patients with stage I or II lung cancer	90	Video-assisted thoracoscopic surgery	Lobectomy	Not specified	30-60
Gonzalez D et al., 2011[10]	Patients with lung cancer, or other non-cancerous lung diseases	200	Video-assisted thoracoscopic surgery	Lobectomy	Not specified	Not specified
Hernandez-Arenas L et al., 2018[11]	Patients with lung cancer with T1 or T2 tumor, N0 or N1 tumor, chest wall involvement of the parietal pleura or ribs, previous thoracic surgery, forced expiratory volume in 1 second of >40% and predicted postoperative diffusing capacity of the lungs for carbon monoxide >40%	60	Video-assisted thoracoscopic surgery	Uniportal lobectomy or segmentectomy	Duration of surgery	26-30
Yu WS et al., 2015[12]	Patients with lung cancer	251	Video-assisted thoracoscopic surgery	Lobectomy	Cumulative Failure	15-40
Decaluwe H et al., 2015[13]	Patients with lung cancer, pulmonary metastasis, or non-neoplastic disease	384	Video-assisted thoracoscopic surgery	Segmentectomy, lobectomy, bilobectomy	Not specified	50
Nakanishi R et al., 2014[14]	Patients with advanced stage non-small cell lung cancer of preoperative stage II or greater	76	Thoracoscopic	Lobectomy or bilobectomy or pneumonectomy	Not specified	25
Vieira A et al., 2020[15]	Patients with stage I or II non-small cell lung cancer	274	Video-assisted thoracoscopic surgery	Lobectomy	Procedure time	141
Cheng YJ, 2015[16]	Patients with lung cancer	56	Two-instrument complete thoracoscopic surgery	Lobectomy	1. Surgery time 2. Lymph node	28

Meyer M et al., 2012[17]	Patients with clinical stage I or II lung cancer	185	Robot-assisted thoracoscopic surgery	Lobectomy	1. Operative time 2. Number of conversions 3. Operative morbidity 4. Operative mortality 5. Hospital stay 6. Surgeon comfort	15 for operative time, 20 cases for operative mortality, 19 cases for surgeon comfort.
Martin-Ucar AE et al., 2017[18]	Patients with primary lung cancer, secondary deposits or non-malignant disease	300	Uniportal video-assisted thoracoscopic surgery	Lobectomy	Not specified	50
Lee EC et al., 2020[19]	Patients with resectable primary non-small cell lung cancer	188 (robot-assisted) 49 (video-assisted)	Robot-assisted thoracoscopic surgery & Video-assisted thoracoscopic surgery	Lobectomy with mediastinal and hilar lymph node dissection	1. Operative time 2. Lymph nodes sampled	20 cases for initial learning curve, 78 cases before reaching competency on par with VATS
Chang CC et al., 2020[20]	Patients with early state lung cancer	364 (segmentectomy) 91 (subsegmentectomy)	Single-port video-assisted thoracoscopic surgery	Subsegmentectomy & segmentectomy	Operative time	28
Toker A et al., 2016[21]	Patients T1a-b, or cT2N1 lesions, or benign lesions in the lung.	100	Video-assisted thoracoscopic surgery	Lobectomy, segmentectomy, & pneumonectomy	Operative time, docking time, console time	14 cases for docking, 13 for console, 14 for operating time
Xiong R et al., 2020[22]	Patients with histopathologically proven non-small cell lung cancer, with no neoadjuvant therapy, clinical T1-2N0-1M0 disease before the operation, and no known disease metastases	160	Video-assisted thoracoscopic surgery	Lobectomy	Operative time and blood loss	40
Fahim C et al., 2017[23]	Patients with non-small cell lung cancer	167	Robot-assisted thoracoscopic surgery	Lobectomy, segmentectomy, nonanotomic (wedge) resection, & bilobectomy	Console time	20
Hernandez JM et al., 2012[24]	Physiologically low-risk patients with early stage lung cancers or metastatic disease in favourable locations	20	Robot-assisted thoracoscopic surgery	Lobectomy	Operative time	Not specified

Zhang Y et al., 2019[25]	Patients with preoperatively biopsied peripheral lung tumor nodules, or nonbiopsied highly suspicious nodules, that are ≤2 cm with at least one of the following: pure adenocarcinoma in situ histology, nodule greater than or equal to 50% ground-glass appearance on CT, and radiologic surveillance confirmation of a long doubling time	104	Robot-assisted thoracoscopic surgery	Segmentectomy	1. Operative time 2. Surgical failure	40 RA-CUSUM, 46 CUSUM
Duan L, Jiang G, & Yang Y, 2018[26]	Patients with benign lung diseases with ground glass opacities, T1N0M0 peripheral lung cancer with tumor diameter ≤2 cm, peripheral lung cancer that would not tolerate lobectomy, ground glass opacities lesions that could not guarantee that the margin would be more than 2 cm by wedge resection, or multiple nodules and bilateral surgery	156	Video-assisted thoracoscopic surgery	Segmentectomy	Not specified	Not specified
Divisi D et al., 2018[27]	Patients with malignant or benign lung tumors, or metastatic disease	3700	Video-assisted thoracoscopic surgery	Lobectomy	1. Operative time 2. Post-operative complications	Not specified
Le Gac C et al., 2020[28]	Patients with lung tumors ≤2 cm, with low-growth features, absence of metastases, and high operative risk	102	Robot-assisted thoracoscopic surgery	Segmentectomy	Operative time	27 cases for CUSUM, 31 for exponential model
Kamiyoshihara M et al., 2013[29]	Patients undergoing mediastinal lymph node dissection	84	Video-assisted thoracoscopic surgery	Lobectomy	Operative time	15
Lee PC et al., 2016[30]	Patients with non-small cell lung cancer	500	Video-assisted thoracoscopic surgery	Lobectomy	1. Number of lymph nodes excised 2. Number of lymph node stations excised	50
Huang CL et al., 2014[31]	Patients with non-small cell lung cancer	87	Video-assisted thoracoscopic surgery	Lobectomy	1. Operative time 2. Blood loss	30
Nachira D et al., 2018[32]	Patients with cN0 or cN1 lung cancers	43	Video-assisted thoracoscopic surgery	Lobectomy	Operative time	25
Wu W et al., 2018[33]	Patients with small peripheral nodules (diameter ≤2 cm) that were (i) adenocarcinoma in situ and (ii) nodules with 50% ground glass	128	Video-assisted thoracoscopic surgery	Lobectomy	Operative time	72 cases for operative time

	opacity on CT; or, patients with poor pulmonary reserve or another major comorbidity that contraindicated lobectomy; or patients with deep indeterminate pulmonary nodules and solitary metastases that were unable to be removed by wedge resection					
Gallagher SP et al., 2018[34]	Patients with early stage non-small cell lung cancer	157	Robot-assisted thoracoscopic surgery	Lobectomy	1. Operative time 2. Conversion to open 3. Estimated blood loss 4. Hospitalization duration 5. Overall morbidity 6. Pathologic Nodal Upstaging	40 cases for conversion to open, 60 cases for operative time
Liu X et al., 2018[35]	Patients with both malignant and benign lesions on the lung	120	Uniportal video-assisted thoracoscopic surgery	Lobectomy	Operative time	44
Chen L et al., 2020[36]	Patients with one of the following: (1) tumour size no more than 2 cm with at least one of those that were pure adenocarcinoma in situ histology, more than 50% ground-glass appearance on CT and radiologic surveillance confirmation of a long doubling time (≥400 days); (2) comprised cardiopulmonary reserve or other complications not suitable for lobectomy; (3) a benign lesion or a metastatic that was inappropriate for wedge resection due to the location in the deep parenchyma of the lung.	123	Uniportal video-assisted thoracoscopic surgery	Segmentectomy	1. Operative time 2. Surgical failure	24 standard CUSUM, 27 RA-CUSUM
Song G et al., 2019[37]	Patients with non-small cell lung cancer	208	Robot-assisted thoracoscopic surgery	Lobectomy (R0 resection)	1. Total operative time 2. Docking time 3. Console time	1. 32 cases 2. 20 cases 3. 34 cases
Hamada A et al., 2018[38]	Patients with primary lung cancer, lung metastases or benign disease	252	Video-assisted thoracoscopic surgery	Segmentectomy	Operative time	32 cases for leading surgeon, 38 cases for non-leading

						surgeons (excluding level 3 segments)
Hernandez-Arenas LA, Guido W, & Jiang L, 2016[39]	Patients with benign lung diseases and patients with lung cancer with T status of tumor <5 cm (T1, T2), N status for tumour N0, FEV1 and DLCO >40% postoperative predicted	200	Uniportal video-assisted thoracoscopic surgery	Segmentectomy and Lobectomy	1. Operative time 2. Conversion rate	85 cases for operative time
Cheng K et al., 2016[40]	Patients with lung tumors	70	Uniportal video-assisted thoracoscopic surgery	Segmentectomy	Operative time	33
Cheufou DH et al., 2019[41]	Patients with malignant lung tumors or bronchiectasis	64	Robot-assisted thoracoscopic surgery	Lobectomy	Not specified	20
Demmy TL et al., 1993[42]	Patients undergoing therapeutic or diagnostic thoracoscopic surgery	69	Video-assisted thoracoscopic surgery		1. mean chest tube duration 2. mean length of stay	Not specified
Gonfiotti A et al., 2016[43]	Patients with non-small cell lung cancer	146	Video-assisted thoracoscopic surgery	Lobectomy	Not specified	50
Ferguson & Walker, 2006[44]	Patients with malignant stage I or II disease in the lung	276	Video-assisted thoracoscopic surgery	Lobectomy	1. Mean operation time 2. Mean blood loss 3. Mean postoperative stay	Not specified
Arnold BN et al., 2019[45]	Patients with lung tumors	101	Robot-assisted thoracoscopic surgery	Lobectomy	Operating time	22 cases for learning phase, 41 cases for continuing development, and 38 cases for mastery
Puri V et al., 2019[46]	Patients with stage I lung cancer	24,196	Video-assisted thoracoscopic surgery	Lobectomy	1. Operative mortality 2. Major morbidity, 3. Blood transfusion.	50
Gezer S, Avci A, & Turktan M, 2016[47]	Patients with malignant or benign lung tumors	58	Video-assisted thoracoscopic surgery	Lobectomy	1. Operative time 2. Hospital stay	27 cases for operative time was not reached for length of stay
Stamenovic D, Messerschmidt A, & Schneider T, 2019[48]	Indication for surgery not described	104	Uniportal video-assisted thoracoscopic surgery	Lobectomy	1. Mean operative time 2. Number of resected lymph nodes	27 cases for operative time (efficiency), 39 cases for mastery 26 cases for lymph node efficiency, 42 for mastery

Baldonado J et al., 2019[49]	Patients with primary lung cancers, or metastatic lung disease	272	Robot-assisted thoracoscopic surgery	Lobectomy with hilar and mediastinal lymphadenectomy	Not specified	Not specified
Smith DE et al., 2015[50]	Patients with lung tumors with a diameter minor of 5 cm, with preoperative knowledge about absence of involvement of great vessels, chest wall or diaphragm	154	Video-assisted thoracoscopic surgery	Lobectomy	1. Operative time (min) 2. Bleeding (mL), 3. VATS conversion	75
Li X, Wang J, & Ferguson MK, 2014[51]	Patients with benign or malignant lung disease	400	Video-assisted thoracoscopic surgery	Lobectomy	1. Operative times 2. Estimated blood loss 3. length of stay	Surgeon A: 157 cases for operative time, 126 cases for estimated blood loss Surgeon B: 108 cases for operative time, 139 cases for estimated blood loss
Terra RM et al., 2019[52]	Indication for surgery not described	203	Robot-assisted thoracoscopic surgery	Lobectomy & segmentectomy	Not specified	30
Karnik N, et al., 2020[53]	Patients with pulmonary nodules, pneumothorax, mediastinal mass, interstitial lung disease, chylothorax, or pericardial effusion	79	Robot-assisted thoracoscopic surgery	Lobectomy	Percentage of cases that were lobectomies (complex thoracic procedures)	Not specified
Aragon J & Mendez IP, 2014[54]	Most patients had non-small cell lung cancer	82	Video-assisted thoracoscopic surgery	Uniportal major pulmonary resection	Not specified	Mean surgical time was reduced after the 40 first cases
Abdellateef A et al., 2020[55]	Patients with primary stage Ia or Ib lung cancer with ground glass opacity of ≤2.5 cm or consolidation ≤1.5 cm, N0 status for the tumor, small benign lung tumors, or localized infectious lung disease	300	Video-assisted thoracoscopic surgery	Subxiphoid uniportal segmentectomy	Operative time	148
Veronesi G et al., 2011[56]	Patients with suspected or proven clinical stage I-III lung cancer	91	Robot-assisted thoracoscopic surgery	Lobectomy	Operative time	18-20

Abbreviations: cm, centimeter; CT; computed tomography, DLCO, diffusing capacity of lung for carbon monoxide; FEV1, forced expiratory volume in one second; CUSUM, cumulative sum; OR, operative time; VATS, video-assisted thoracoscopic surgery; RA-CUSUM, risk-adjusted cumulative sum.

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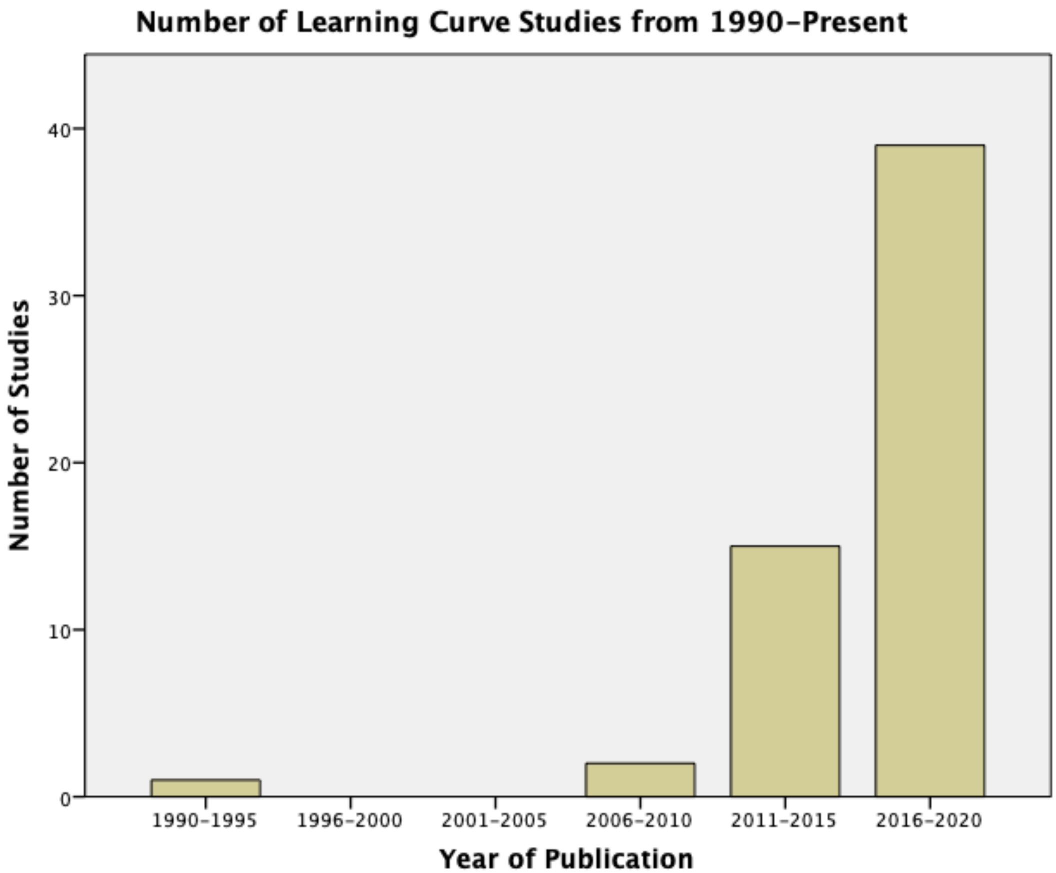
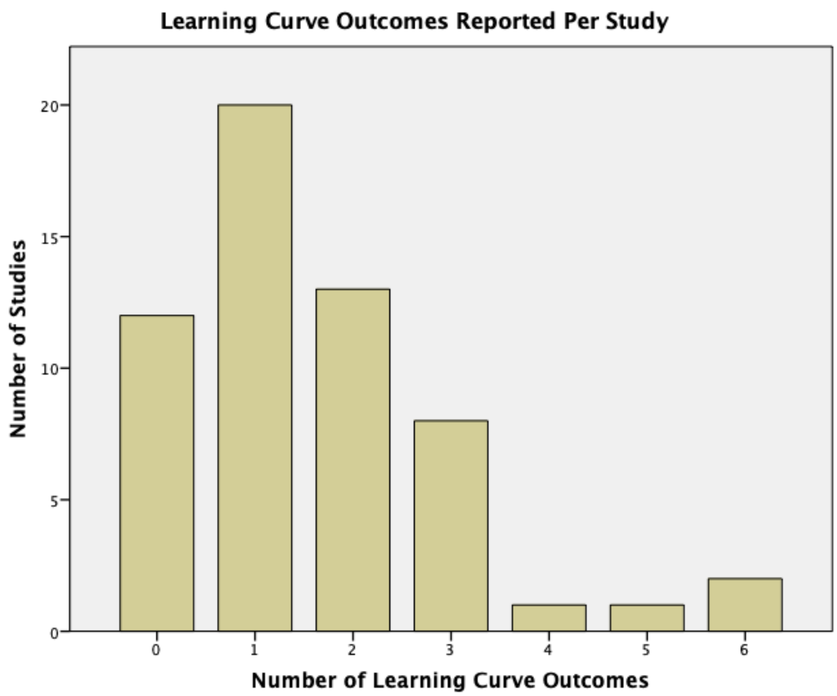
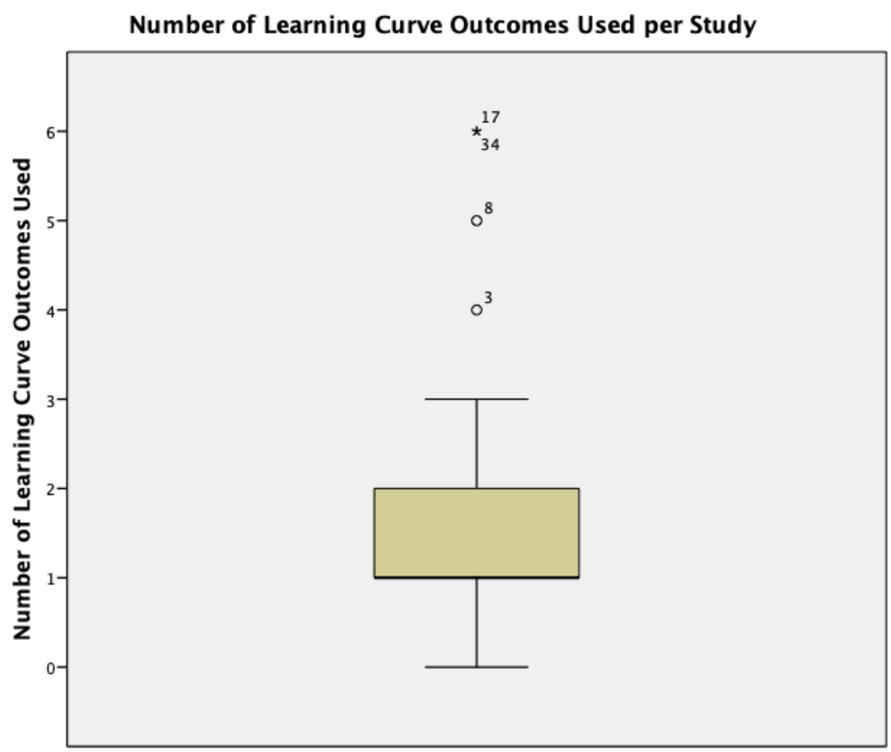
Appendix 6. Number of Learning Curve Studies from 1990-Present



Appendix 7. Learning Curve Outcomes Reported Per Study





CHAPTER II

LEARNING CURVE ANALYSIS OF NEAR-INFRARED FLUORESCENCE GUIDED ROBOT-ASSISTED SEGMENTECTOMY WITH INDOCYANINE GREEN DYE USING CUMULATIVE SUM METHODOLOGY

ABSTRACT

Introduction: Robotic pulmonary segmentectomy is a technically demanding procedure requiring intraoperative identification of intersegmental plane anatomy. Near-infrared fluorescence (NIF) mapping using Indocyanine Green dye has been shown to assist with intersegmental plane identification, however, the learning curve of this procedure has yet to be characterized. The objective of this trial was to evaluate the learning curve of this novel procedure.

Methods: Adults diagnosed with early-stage non-small cell lung cancer, and a tumour ≤ 3 centimetres in diameter confined to a single bronchopulmonary segment received NIF-guided robot-assisted segmentectomy using the completely portal 4 arm approach (CPRS-4). Cumulative sum analysis was used to evaluate the learning curve, with operative time as the outcome. The inflection point which signals attainment of competency was identified through visual inspection.

Results: The trial recruited 177 participants between October 2016 and January 2021, of which 106 received NIF-guided CPRS-4 and included a roughly equal distribution of simple (51/106, 48.11%) and complex (55/106, 52.81%) cases. The inflection point of the learning curve for NIF-guided CPRS-4 occurred following the 62nd case, after which point clinically important reductions in blood loss (Phase 1=127.73 mL vs. Phase 2=102.32 mL; p<0.001) and operative time (MD=16.9 minutes; 95%CI 5.95, 27.85; p=0.003), as well as an increase in lymph node yield was observed, despite similar distribution of complex and simple segments among the learning phases. This study reports the first learning curve characterization of NIF-guided CPRS-4, which appears to be around 62 cases before the surgeon reaches a plateau in performance.

Conflicts of Interest: None.

Funding Source: Boris Family Centre for Robotic Surgery.

INTRODUCTION

Surgery for Non-small Cell Lung Cancer

Segmentectomy is a parenchyma-sparing technique that has been proposed for the treatment of early-stage non-small cell lung cancer (NSCLC). Anatomically, lungs are comprised of five lobes, which can be further divided into smaller anatomical components called broncho-pulmonary segments. Each segment contains its own blood supply, therefore each segment is functionally and physiologically independent. For patients who have a tumour confined to one broncho-pulmonary segment, the removal of a particular segment—called a segmentectomy—is possible. Advances in computed tomography have led to an increase in the screening and early detection of NSCLC and has driven the demand for segmentectomy,[1] which retains more healthy lung tissue when compared to the removal of an entire lobe of lung (lobectomy). Therefore, patients with small tumours (≤3cm in diameter), compromised lung function, or bilateral pulmonary nodules requiring multiple resections over time stand to benefit the most from segmental resections.[2]

Despite these notable advantages, segmentectomy remains a controversial procedure to perform for a number of reasons. Firstly, segmentectomy is technically demanding. Variation in segmental anatomy[3] and indiscriminate anatomical structures within the lung tissue[4] can introduce variability when performing the procedure. Secondly, segmentectomy may require the identification of multiple intersegmental planes and the obtainment of safe resection margins in several lung surfaces. This factor can contribute to concerns of insufficient margin length and potential tumour recurrence at the resection margin, and presents a particular challenge in the context of malignant disease. Finally, higher rates of mortality and morbidity, including prolonged air leak, longer length of hospital stay, and prolonged chest tube duration (>5 days) have been highlighted as additional patient safety concerns for performing this procedure over other types of anatomical lung resections.[5] Many of these concerns have drawn their basis from a historical trial performed in 1995 by Ginsberg et al., who reported a three-fold increase in regional recurrence and inferior survival associated with segmentectomy when compared to lobectomy.[6] While this seminal study set the standard of care for early stage NSCLC, it was conducted using crude segmentectomy techniques, it pooled segmentectomy and subsegmentectomy (wedge) resections together, and minimally invasive surgical techniques had not yet been popularized. As a result, many patients who would otherwise be candidates for segmentectomy, undergo a full lobectomy, even when it may not be clinically necessary.[7]

Advances in Segmentectomy Techniques

Contemporary evidence suggests that segmentectomy has equivalent survival to lobectomy,[8] and may even lead to better patient outcomes including: less blood loss, shorter operation time, less chest tube drainage, and shorter length of stay.[9] While there are at least two prospective clinical trials currently assessing the clinical efficacy of segmentectomy,[10,11] approaches to lesion localization and resection via segmentectomy have progressed considerably since the landmark trial by Ginsberg and colleagues.

Anatomical segmentectomy has shown to be feasible using both multi-port and uniport[12] video-assisted thoracoscopic surgery,[13] in addition to more recent advancements on the robotic surgical platform.[14] Innovative methods of preoperative lesion marking and intraoperative margin assessment techniques have aided in the adoption of this challenging procedure.[15]

Hanna and colleagues[16] recently described one of these advancements using near-infrared fluorescence (NIF) and indocyanine green (ICG) dye. In NIF-guided robot-assisted segmentectomy, an intravenous injection of the dye travels through the lungs and illuminates with a fluorescent green hue when exposed to near-infrared light. In this way, the surgeon is able to isolate the entire lung except the segment planned for removal by ligating and dividing the inflow and outflow vessels of the target segment prior to injection. This novel technique, originally described by Pardolesi et al., has been used to localize segments through visual delineation of the segmental anatomy.[17] In a trial of 80 patients, Hanna et al. found significantly lengthened resection margins in addition to feasible identification of segmental plane anatomy with NIF-guided segmentectomy.[16] While this finding indicates added value of NIF-guided resection, the learning curve has not yet been evaluated for this novel procedure.

Learning Curves for Major Thoracic Robotic Procedures

While the previously discussed issues of heterogeneity between individual learning curve evaluations described in Chapter 1 preclude between-study comparisons and/or pooling of data to estimate an average learning curve of a given surgical procedure, a number of investigations have described the experience required to safely perform major thoracic procedures. The learning curve for robotic thymectomy appears to be 10-20 cases[18-20], while the learning curve for anatomic robotic lung resections are much more variable. The results from several studies indicate significantly shorter operative times after reaching 20 cases,[21-25] while other studies suggest slightly longer learning curves of at least 40-60 cases before proficiency is reached[26,27]. Interestingly, Fahim et al. noted a higher rate of conversion to thoracotomy with increasing case numbers in Canada's first case series of robot-assisted thoracoscopic surgery[21]. This has been hypothesized to be due to the fact that surgeons are willing to perform difficult resections on more central tumours as they become increasingly comfortable with the surgical technique.

Therefore, the current literature suggests that the learning curve for anatomical lung resection ranges between 20 and 40 cases. With regards to the learning curve of robot-assisted segmentectomy, Zhang et al. have demonstrated that the learning curve is overcome after 41 cases[27].

However, the learning curve associated with NIF-guided robot-assisted segmentectomy is not currently known. Thus, there is a need to characterise the learning curve of this procedure in order to evaluate its feasibility for physician uptake. We sought to perform a CUSUM analysis of the learning curve for robot-assisted segmentectomy with and without NIF-guidance, which will be the first quantitative assessment of this novel procedure. To the author's knowledge, this study will be the first North American description of the learning curve for anatomical lung resection using the robotic approach. The results will report the number of cases required to perform robot-assisted segmentectomy using NIF mapping as a surgical adjunct, identify potential barriers to physician uptake, and help promote safe adoption of minimally invasive robotic procedures.

Study Aims

The purpose of this project was to perform a CUSUM analysis in order to determine the number of cases needed to overcome the learning curve of robot-assisted segmentectomy, with and without NIF-guidance with ICG dye, by a single surgeon experienced in minimally invasive techniques.

The learning curve will be described in different phases indicated by distinct and sustained changes in surgeon performance. Typically, these phases are characterized by (1) a starting point, where individual level factors such as initial experience and personal expertise provide a baseline level of competency, (2) a slope period, which is determined by the speed by which one learns a new task, and (3) a plateau, where the incremental change in the outcome being measured becomes marginal. Technical proficiency will be considered the inflection point in the learning curve where surgeon performance reaches a plateau (i.e. minor changes are observed in the process variable). The secondary aims of this study are to compare clinical outcomes of (1) patients belonging to different phases of the learning curve, as identified through CUSUM analysis and (2) to assess differences in patients with simple versus complex segmental resections.

We hypothesized that significant differences in operative time and conversions to lobectomy and/or thoracotomy, will be observed across the initial and final learning curve phases. In addition, we hypothesized that using the NIF ICG surgical adjunct will require fewer cases before overcoming the learning curve.

METHODS

Ethics

This study was granted a no objection letter from Health Canada authorizing the off-label use of ICG (#184323) and was approved by the Hamilton Integrated Research Ethics Board. The study was carried out in compliance with the Canadian Tri-Council Policy Statement on Ethical Conduct for Research Involving Human Subjects.[28] Participants provided full informed consent for the surgery and associated study procedures. The trial was registered on www.clinicaltrials.gov (#NCT02570815).

Study Design

This was a single-centre trial that assessed a prospective cohort of patients undergoing robotic segmentectomy with and without the use of a NIF-guided surgical adjunct between October 2016 and January 2021. Methods and results from the first 80 patients from this cohort have already been reported.[16] Participants providing their consent had their demographic, clinical, and follow-up data analyzed. Patients were assessed chronologically for the learning curve analysis. Perioperative outcomes of each patient among the learning curve phases are summarized and compared between phases using descriptive and inferential statistical analyses.

Patient Population

As has been previously described,[16] we enrolled individuals who are older than 18 years of age, with clinical stage I NSCLC and a tumour ≤3 cm in diameter that is confined to one broncho-pulmonary segment confirmed by CT imaging, rendering the candidate suitable for robotic segmentectomy. Individuals receiving lobar or non-robotic segmental resections were not eligible for this study. It is unknown if ICG dye has teratogenic effects or is excreted in human breast milk,[29] therefore, pregnant and/or breastfeeding women, or women of childbearing potential and who are not taking adequate birth control were excluded. Individuals with sensitivity or intolerance to contrast dye were also excluded.

All participants were operated on by a single surgeon (WCH) using the da Vinci System (Intuitive Surgical, Sunnyvale, CA) at a tertiary medical centre in Hamilton, Ontario, Canada. Prior to adopting the robotic segmentectomy approach described in this study, the surgeon had performed over 500 video-assisted thoracoscopic lobectomies and more than 250 robotic cases, but no prior robotic segmentectomies. Patients consenting to the study were prospectively enrolled prior to operation and were followed for 30 days postoperatively. Imaging data were reviewed jointly by a radiologist and the operating surgeon to determine where the primary lung nodule and corresponding pulmonary vein, and artery were located.

Peri-Operative Outcome Measures

Operative time, defined as the time between the start of surgery and skin closure, was the metric used to assess the proficiency of NIF-guided robotic segmentectomy. This parameter was selected *a priori* as it is the most commonly reported measure used to assess learning curves in the thoracic surgical literature (Chapter 1).

Intra- and postoperative metrics were also measured and collected. Intraoperative information, such as rates of conversion to lobectomy and thoracotomy, blood loss, and additional post-operative surgical complications as per the Ottawa Thoracic Morbidity and Mortality System for Classifying Thoracic Surgical Complications (TM&M) were collected.[30] TM&M is a well-established and standardized classification system for reporting adverse events after surgery. It provides definitions, categories, and severity of complications. In addition, blood loss, chest tube drainage, and operation time was also collected prospectively from anesthesia records. Length of hospital stay was be obtained from hospital records. Participants were followed up over a 30-day period, where study visits will coincide with routine 2- and 4-week clinic follow-ups in accordance with institutional protocols. Pathology details, including pathological stage, number of lymph nodes sampled, tumour size, and tumour location were also collected from the pathology note of each participant. The TNM staging system was used for cancer staging.[31]

Segment Complexity

To control for differences arising from more challenging resections based on tumour location, each operation was classified into two categories according to the degree of segmental complexity. The definition used to categorize simple and complex segments is consistent with previous literature and based on the number of intersegmental dissection surfaces encountered during resection.[32] Each segmental resection was classified as either simple (a single or minimal intersegmental dissection surfaces), or complex (multiple dissection surfaces in contact at obtuse angles) (Appendix 1).

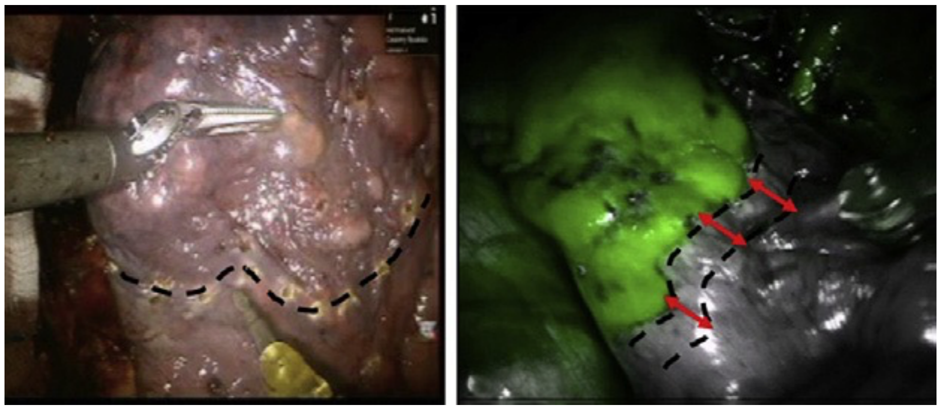
Operative Technique

As has been previously described,[16] all operations were conducted by a single surgeon using the da Vinci robotic platform (Intuitive Surgical, Sunnyvale, California) using the Completely Portal 4-Arm (CPRS-4)[33] approach and Firefly Fluorescence Imaging camera (Intuitive Surgical) as a light source for NIF. Conversion to lobectomy was necessitated when

N1 disease was suspected or confirmed on intraoperative frozen section, when negative margins could not be obtained, or when the tumour was missing from the resected specimen. Conversions to thoracotomy were indicated when the procedure failed to progress robotically or when required due to intraoperative complications.

At the time of surgery, the surgeon ligated the pulmonary vein and artery of the broncho-pulmonary segment containing the lung cancer nodule, isolating the in- and out-flow blood vasculature. The lung parenchyma of the isolated segment then displayed a purple discoloration consistent with ischemia. ICG was prepared as a sterile solution (2.5 mg/10mL) for injection, as per the protocol used in previous case reports.[17] After vascular ligation, a 6 to 8mL bolus of ICG solution was injected into the peripheral vein catheter, followed by a 10-mL saline solution bolus, as described by Pardolesi et al.[17] The Firefly camera, capable of detecting infrared fluorescence, was then be used for lung imaging using the NIF adjunct. The entire lung, except the broncho-pulmonary segment which was previously isolated from blood supply, then fluoresces within 30-40 seconds, exhibiting a green hue.[17] The border between the 'dark' segment and the adjacent fluorescent lung parenchyma served as the visual cue to the true anatomical inter-segmental plane (Figure 1). The surgeon then proceeded with the pulmonary resection along this inter-segmental plane. The resected 'dark' lung segment was immediately evaluated by a pathologist on-site. If the lung nodule of interest was located within the segment, and the resection margins were free of tumour, then the operation was concluded. If the lung nodule was not located within the segment, or if the margins of resection were positive for malignant tumour, then the patient would receive a pulmonary lobectomy to ensure successful resection of the nodule.

Figure 1. Demonstrating extension of margins by ICG mapping: Identification of bronchopulmonary segment (dark) and the surrounding healthy tissue (green).



Statistical Analysis

Cumulative Observed-Expected Failure Chart

The CUSUM method is a recursive quality monitoring tool used to measure the sum of deviations between the individual data points and the mean of all data points[34]. The CUSUM approach is advantageous to other audit methods since it allows for the sensitive detection of slow sustained degradation of a process otherwise thought to be under control[35].Operative time, as defined earlier, will be used as the parameter for CUSUM ($CUSUM_{OT}$), specified here as $\boldsymbol{CUSUM_{OT} = \sum_{i=1}^{n}(x_i - \mu)}$, where x_i indicates an individual operative time and μ indicates the mean operative time. Patients were assessed chronologically based on their operation date, beginning with the earliest case and ending with the latest case. A total of four CUSUM graphs were generated in this analysis. Two CUSUM curves were generated for patients who undergo either NIF-guided or standard robot-assisted segmentectomy. For those who receive the ICG injection, an additional two CUSUM charts were graphed based on segment complexity (simple and complex). If performance was favourable, the CUSUM line trended downward. Distinct deviations in performance, as measured in excursions from the process variable mean, signalled a departure from a previous phase and entry into a new phase of the learning curve. The inflection point on the graph was used to identify when the learning curve had been overcome.

Segment Complexity and Interphase Comparisons

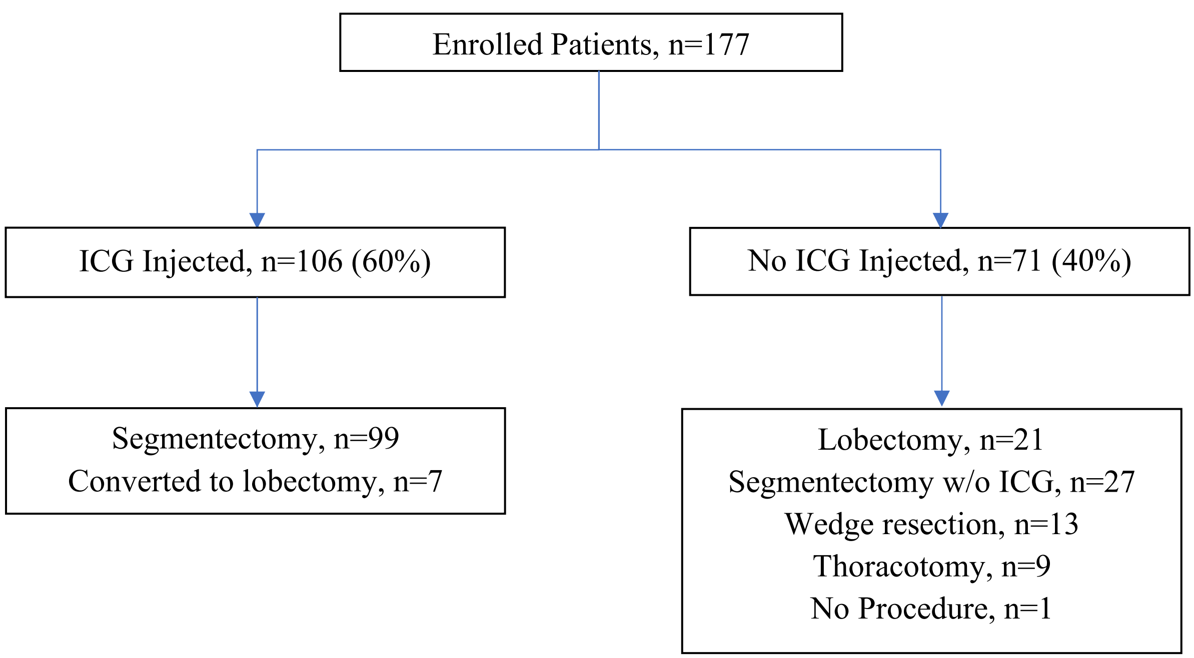
Phases that are generated from the learning curve analysis were used to inform group comparisons of primary and secondary outcomes. Normally distributed continuous variables, as determined through visual inspection of a histogram, were described using means and standard deviations, and group values will were compared using independent sample t-tests. Categorical variables were described using counts and frequencies and compared using the Fischer's exact test. Ordinal variables and non-normally distributed variables were described as median and interquartile ranges and compared using Mann-Whitney U-test. Statistical significance will be set to $p<0.05$. All statistical analysis were performed on SPSS version 22.0 (SPSS Inc. Chicago, IL, USA) software.

RESULTS

Patient Characteristics

One-hundred and seventy-seven patients were enrolled in the trial between October 2016 and January 2021 (Figure 2). Most patients received the planned operation with ICG injection (106/177, 59.9%). The remaining patients who did not receive ICG injection (71/177, 92.21%) underwent segmentectomy (27/71; 38.03), lobectomy (21/7, 21.58%), wedge (13/71, 18.31%), or thoracotomy (9/71; 12.70%), or no procedure (1/71; 1.41%). The surgery for one patient was aborted until further pathology details were made available due to significant existing morbidity.

Figure 2. Consolidated Standards of Reporting Trials diagram.



Reasons for not receiving the dye included visible tumour and/or segmental plane anatomy (15/71, 21.13%); anatomic considerations including dense adhesions (23/71, 32.39%); benign disease (2/71, 2.82%); failure to ligate segmental vasculature (12/71, 16.90%); bronchial or vascular injury (4/71; 5.6%); uncertain tumour etiology (1/71, 1.41%); inability to tolerate single-lung ventilation (1/71, 1.41%); inability to secure adequate oncologic margin (8/71, 11.27%); metastatic disease (3/71, 4.22%); significant existing morbidity (1/71; 1.41%) and segmentectomy not required (1/71, 1.41%).

Participant characteristics are summarized in Appendix 2. Participants in the ICG and non-ICG groups did not exhibit any statistical differences in age, sex, BMI, smoking status, comorbidities, cancer history, forced expiratory volume in one second (FEV1), predicted diffusing capacity of lung for carbon monoxide (%DLCO), and disease characteristics. There was a single mortality in the ICG group after experiencing a vascular event.

When compared to patients receiving ICG segmentectomy, the operative time of those receiving standard segmentectomy was significantly shorter (mean difference (MD) = -13.07 minutes; 95% confidence interval (95% CI) -22.69, -3.45); p=0.008). Patients receiving standard segmentectomy were also more likely to have a completion lobectomy (ICG=6.60% vs. non-ICG=32.40%; p<0.001), be converted to thoracotomy (ICG=1.89% vs. non-ICG=22.54%; p<0.001), have additional lung procedures performed (ICG=24.53% vs. non-ICG=40.85%; p=0.031), and have less lymph nodes sampled (ICG= 7 IQR, 5-9 vs. non-ICG=6 IQR 4-8; p=0.008). Segment complexity distribution between ICG and non-ICG patients were equal (p=1.00). Full surgical details are presented in Appendix 3.

Learning Curve Analysis

Visual inspection of the CUSUM plot of operative time revealed that the learning curve of segmentectomy with ICG dye was overcome after 62 procedures (Figure 3a). In comparison, the learning curve of segmentectomy without ICG dye was overcome after 26 procedures (Figure 3b). The inflection point of the CUSUM curve demarcates a change in the overall slope of the curve from a general positive slope (Phase 1) to a negative slope (Phase 2). While a positive slope indicates that the surgeon takes longer than average to complete the operation, a negative slope indicates that the surgeon's operative times are decreasing below the average value. As such, the inflection point represents a shift from increasing to decreasing operative time, and signifies that the surgeon has attained proficiency in the operative technique as he is now able to perform it more efficiently.

Figure 3a. CUSUM$_{OT}$ Plot for ICG Segmentectomy

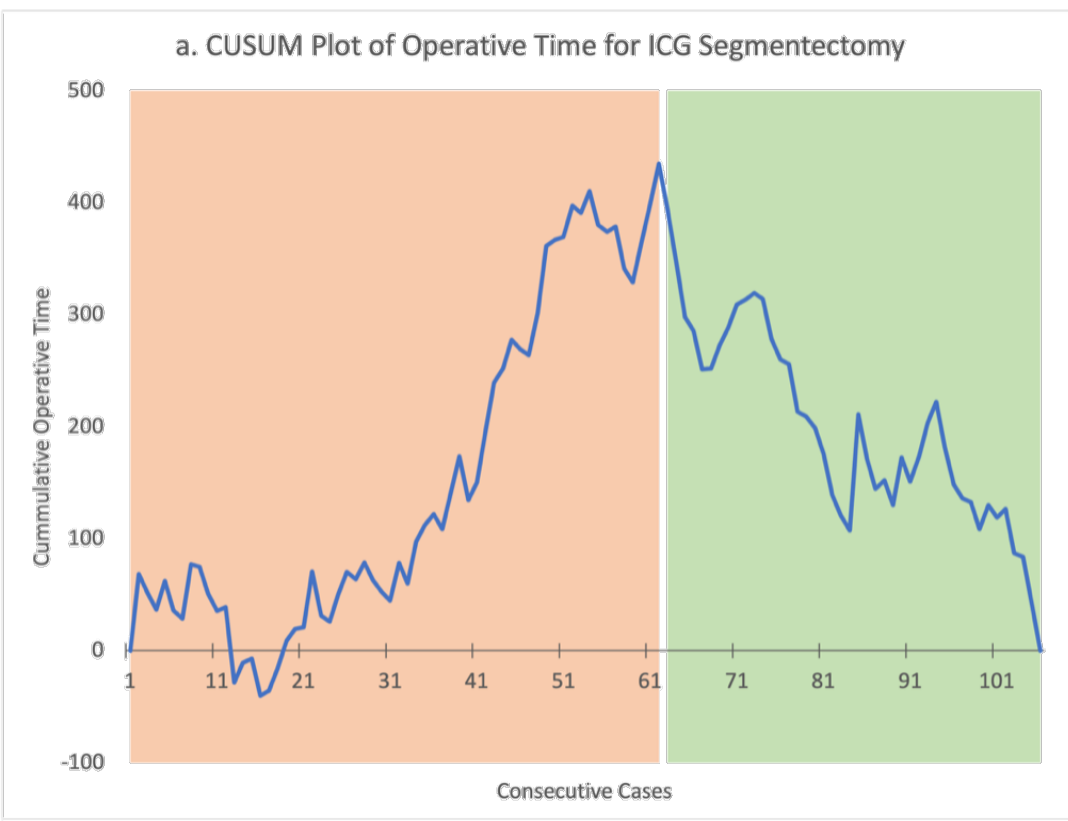
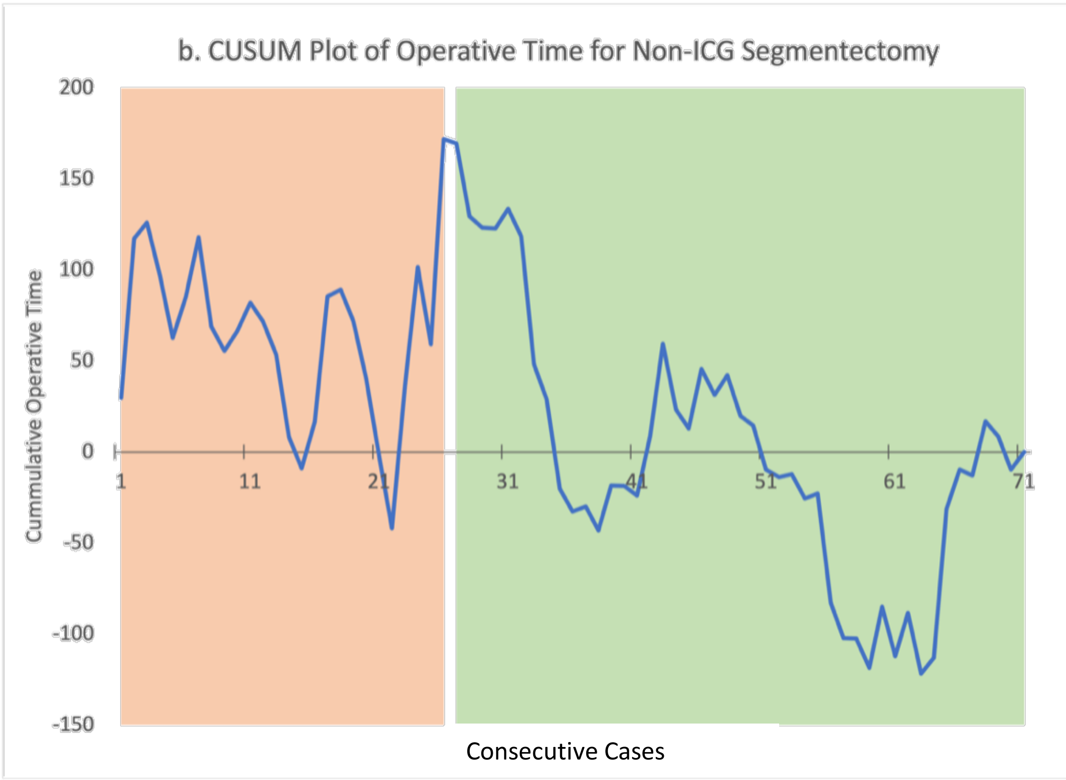


Figure 3b. CUSUM$_{OT}$ Plot for Non-ICG Segmentectomy



As shown in the Cumulative Sum (CUSUM) curves, cut-off points were observed on (a) the 62nd case in ICG patients, and following (b) the 29th case for non-ICG patients due to an increase and a decrease in the operative time. Phase 1 (red) indicates when the curve was ascending (positive cumulative operative time), suggesting that the operative time was still longer than the average operative time. Phase 2 (green) indicates when the curve had a tendency to decline (negative cumulative operative time), indicating that the operative time was shorter than the average operative time.

In comparing the learning curve of segmentectomy with ICG dye between simple and complex cases, a similar number of cases were needed to overcome the learning curve. Thirty-three cases were needed for complex segmentectomies with ICG (Figure 4a), while a slightly lower threshold of 29 cases was required for simple segmentectomies with ICG (Figure 4b).

Figure 4a. $CUSUM_{OT}$ Plots for Complex Cases

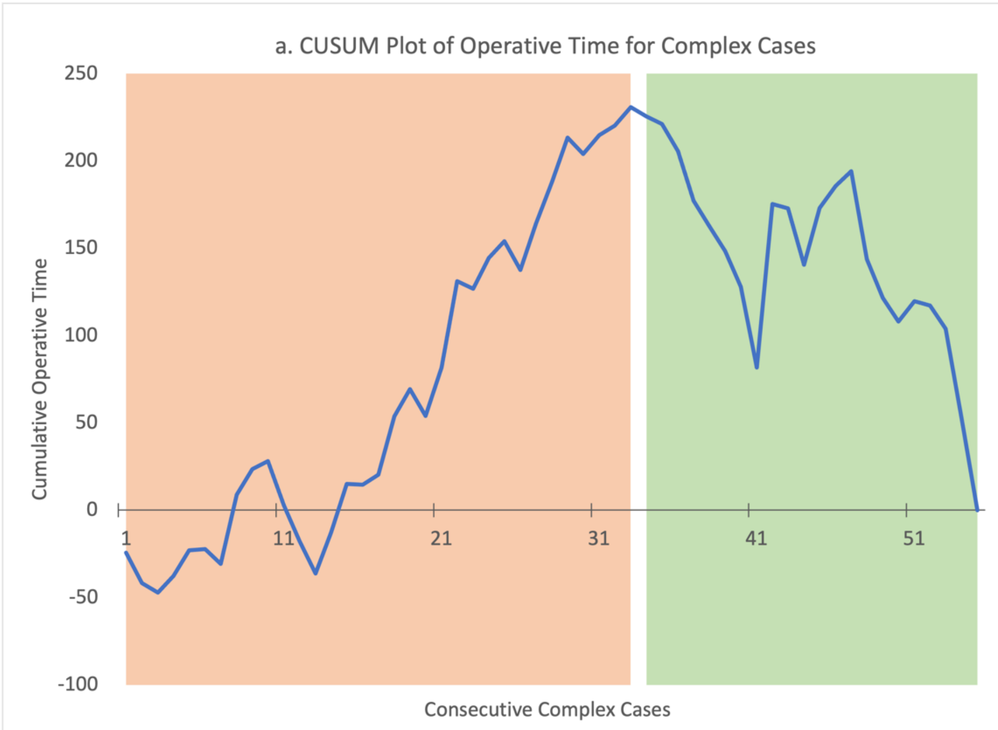
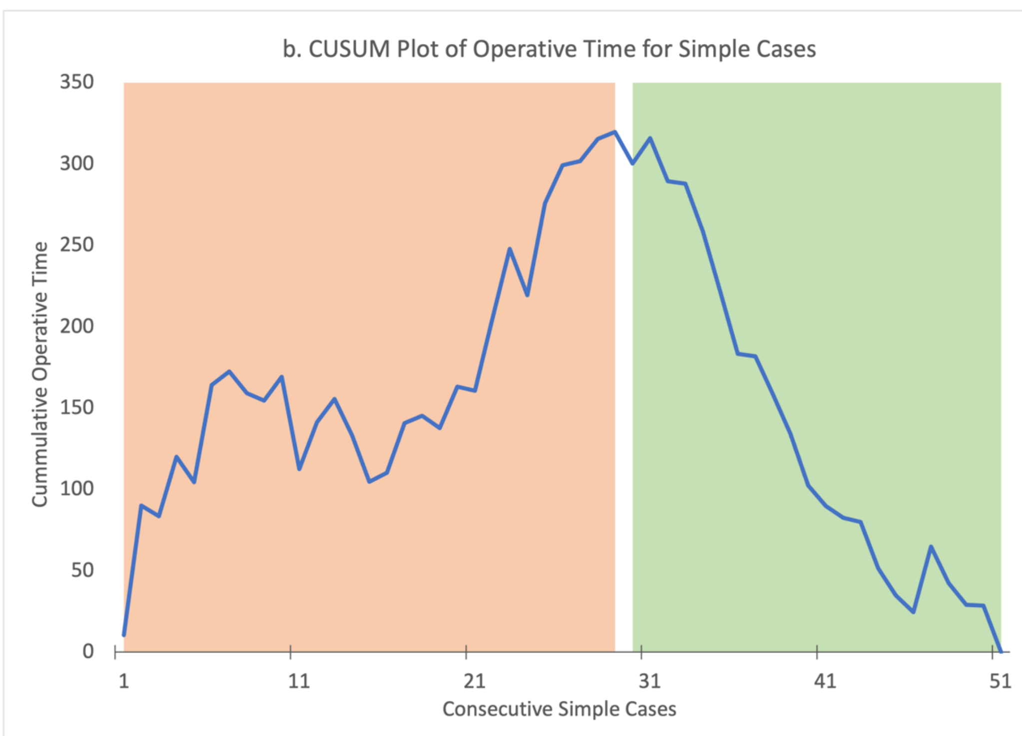


Figure 4b. $CUSUM_{OT}$ Plots for Simple Cases



Perioperative Outcomes Compared Among the Learning Phases

Comparison of operative time between learning phases of ICG segmentectomy cases revealed significantly longer operative time in Phase 1 (MD=16.9 minutes; 95%CI 5.95, 27.85; p=0.003) when compared to Phase 2, despite similar distribution of case complexity between the phases (Appendix 4). Furthermore, participants in Phase 2 experienced significantly less blood loss (Phase 1=127.73 mL vs. Phase 2=102.32 mL; p<0.001) and more extensive lymph node dissection (Phase 1= 6 IQR, 4-6 vs. Phase 2=8 IQR, 6-8; p=0.023). The participants in Phase 1 and 2 differed significantly in the distribution of resected lung lobes; a significantly higher proportion of segments belonging to the right upper lobe were resected following the 62nd case, once the learning curve was overcome (Phase 1= 4.84%, vs Phase 2=31.82%). Phases were otherwise similar in other surgical outcomes such as rate of intraoperative complications and adverse events, conversion rate, and rates of additional lung surgery.

Segment Complexity

Comparisons of surgical complexities are summarized in Appendix 5. All ICG segmentectomy cases were divided into two categories based on segment complexity, defined *a-priori*. This included a roughly equal distribution of simple (51/106, 48.11%) and complex (55/106, 52.81%) cases. Simple cases required significantly shorter operative time when compared to complex cases (MD=-20.91 minutes; 95%CI -31.42, -10.40, p<0.001). Complex cases were more likely to receive more extensive lymph node dissection as measured by number of lymph nodes sampled (simple=6.0 IQR, 4-8 vs. complex=8.0 IQR 6,10.5). Intraoperative complications, blood loss, adverse events, conversions, and length of stay were similar in either complexity group.

DISCUSSION

We report the first learning curve evaluation for NIF-guided robot-assisted segmentectomy to be around 62 cases. While many investigations have sought to describe the learning curve for performing video-assisted segmentectomy, the use of robotic surgery in performing sublobar resections is a more recent innovation[36] that requires careful study and evaluation. Through our CUSUM analysis, we demonstrate that cases who were operated on after the 62nd case experienced less blood loss, more extensive lymph node dissection, and shorter operative time than those earlier in the learning curve. Segment complexity was not shown to impact the rate of conversion to open thoracotomy or lobectomy, however, complex cases were associated with longer operative time. In non-ICG cases, the learning curve was overcome after 26 cases, and was associated with more conversions and less extensive lymph node dissection compared to cases operated on using the NIF surgical adjunct.

In this study, the number of cases required to overcome the learning curve for NIF-guided segmentectomy was 62 cases, which is higher than previous reports despite similar rates of conversion.[27] Zhang et al.'s learning curve analysis of robotic segmentectomy features similar CUSUM methodology and reports that proficiency is reached following the 41st case. We believe one of the reasons for the observed differences in the learning curve is due to the higher proportion of complex cases in the present study (51.89% vs. 30.77%), which was significantly associated with longer operative times ($p<0.001$). Furthermore, Zhang et al.'s study does not involve the use of the NIF surgical adjunct which requires additional technical skill to master. More recently, Le Gac et al. reported a learning curve of 30 cases, though their investigation did not account for segment complexity.[14] It is well recognized that learning curves are highly operator dependent,[37] however, our results are in line with other investigations that report a similar learning curve of around 63 cases for robotic anatomic lung resection.[27,38,39]

One of the challenges in using the robotic platform is a lack of tactile feedback when compared to using open approaches, which removes the ability of the surgeon to physically manipulate pulmonary anatomy.[40] This limitation, combined with variations in plane anatomy in the lung, makes the correct identification of segmental plane anatomy a particular challenge in minimally invasive lung surgery. Intraoperative lesion and segmental plane localization through the use of surgical adjuncts have been developed to assist the surgeon in overcoming this technical limitation. Three-dimensional reconstruction on the robotic platform, inflation-deflation using a jet ventilator, and angiography and bronchography are intraoperative methods that have been previously described to detect the intersegmental plane.[1,14,41] To the authors knowledge, this learning curve study is the first to report on the use of ICG dye as a surgical adjunct for delineating plane anatomy in robot-assisted segmentectomy.

The mean operative time and blood loss for NIF-guided robot-assisted segmentectomy was 132.34 minutes and 111.19 milliliters (mL), respectively, which is in line with other reports in the literature. As the surgeon progressed past the 62^{nd} case of the learning curve, blood loss (127.72 mL vs. 102.32 mL, $p=0.007$) and operative time (139.35 minutes vs. 122.45 minutes, $p=0.003$) decreased significantly, and the number of lymph nodes dissected increased significantly (6.00 vs. 8.00, $p=0.023$). While there exists a number of systematic reviews and meta-analyses documenting the safety of sublobar resections compared to standard lobectomy using robot-assisted thoracoscopic surgery, the reporting is concerned primarily with oncologic efficacy and survival data.[42-45] However, our experience is in line with a review published by Cao et al.[46], who report blood loss and operative time ranges well within our values. In addition, extensive lymph node dissection has been shown to be an important prognostic factor in sublobar resections.[47] Therefore, we believe that the learning curve obtained in our study suggests important changes in performance that are associated with marked improvements in clinical outcomes.

Due to the variable anatomic structures involved in pulmonary segmentectomy, we decided to control for segment complexity in our CUSUM analysis of ICG cases. Many factors, such as case-mix and complexity, may influence the ease of which a surgery is performed, and thus the resultant learning curves generated from empirical analysis. Therefore, it is important to control for pre-surgical risk when evaluating the learning curve, wherever possible. Risk-adjusted CUSUM methodology has been developed for this very purpose,[48] however, these analyses depend on the validity of the data-sets of which pre-surgical risks are ascertained as well as the odds ratio and control limits that the learning curve analysis is designed to detect.[49] We chose to evaluate the impact of segment complexity, as more complex segments have been shown to increase operative times when performing minimally invasive segmentectomy.[5] Notably, complex cases required significantly longer operative times than simple cases (142.4 minutes vs. 121.49 minutes, $p<0.001$). Increased number of lymph nodes sampled in complex cases may be a contributory reason for this finding. Interestingly, there were no differences in rates of conversion to thoracotomy or lobectomy in complex segments, as has been reported in other evaluations in both video-[50] and robot-assisted approaches.[7]

Furthermore, the number of right upper lobe (RUL) resections performed in Phase 2 of the learning curve is important to note. Segments comprising the right upper lobe are technically challenging, and the increase of these procedures in Phase 2 suggests the surgeon becoming more comfortable with advancing to more complex cases. Indeed, this is a finding that was absent in a previous report of the first 80 patients in the present trial.[16] In addition, the number of RUL performed with ICG were greater than with non-ICG segmentectomy, indicating that NIF mapping may play an important role in added surgeon confidence in the context of increasing case complexity. This hypothesis is supported by significant increases in conversions to lobectomy and thoracotomy when performing segmentectomies without NIF mapping ($p<0.001$).

This study has multiple shortcomings. First, we acknowledge the lack of inclusion of control limits in our CUSUM analysis of the learning curve. In anticipation of this analysis, the study author conducted a systematic review of surgical learning curves in minimally invasive thoracic surgery, including studies that have evaluated robotic segmentectomy. Unfortunately, due to procedure novelty in addition to perceived heterogeneity of methods used to characterize surgical learning curves in this discipline, we were unable to derive expected values from the literature in which we could base a suitable competency threshold. However, this study provides the requisite data for future novice surgeons who would like to adopt this procedure. Second, we cannot exclude the possibility of selection bias. Although the distribution of lobes were similar between both trial arms, patients were not randomized as is accomplished by conventional interventional trials. Therefore, more complex cases were likely selected later in the learning curve as the surgeon gained sufficient experience with less complex cases. Last, the CUSUM method adopted relies on subjective assessment of the graphs generated, and there is a possibility that they may have been overinterpreted, thus the results may not be generalizable to other surgeons. However, we believe that this study has employed a number of methods to mitigate the potential for this bias. Our learning curve evaluation was structured using explicit definitions and included previous surgeon experience to allow for the contextualization of results to surgeons from different backgrounds of expertise. Our CUSUM analysis also controls for segment complexity, which is an important consideration due to the variations observed in segmental anatomy.

CONCLUSION

Our study sought to describe the learning curve for a novel procedure involving NIF mapping during robot-assisted segmentectomy. CUSUM analysis indicates that the learning curve for NIF-guided robot-assisted segmentectomy can be overcome after 62 cases, after which point clinically important reductions in blood loss and operative time, as well as an increase in lymph node yield, is observed. As lung cancer screening becomes more widely adopted, and early-stage NSCLC comprises the majority of surgeon caseloads, the propensity to perform lung-preserving operations, such as segmentectomy will predominate. Surgical adjuncts such as NIF are enabled by the robotic surgical platform and may facilitate complex procedures such as segmentectomy. Thus, learning curve studies evaluating competency in the context of innovative surgical technologies will be an important part of monitoring patient safety and physician proficiency in the future.

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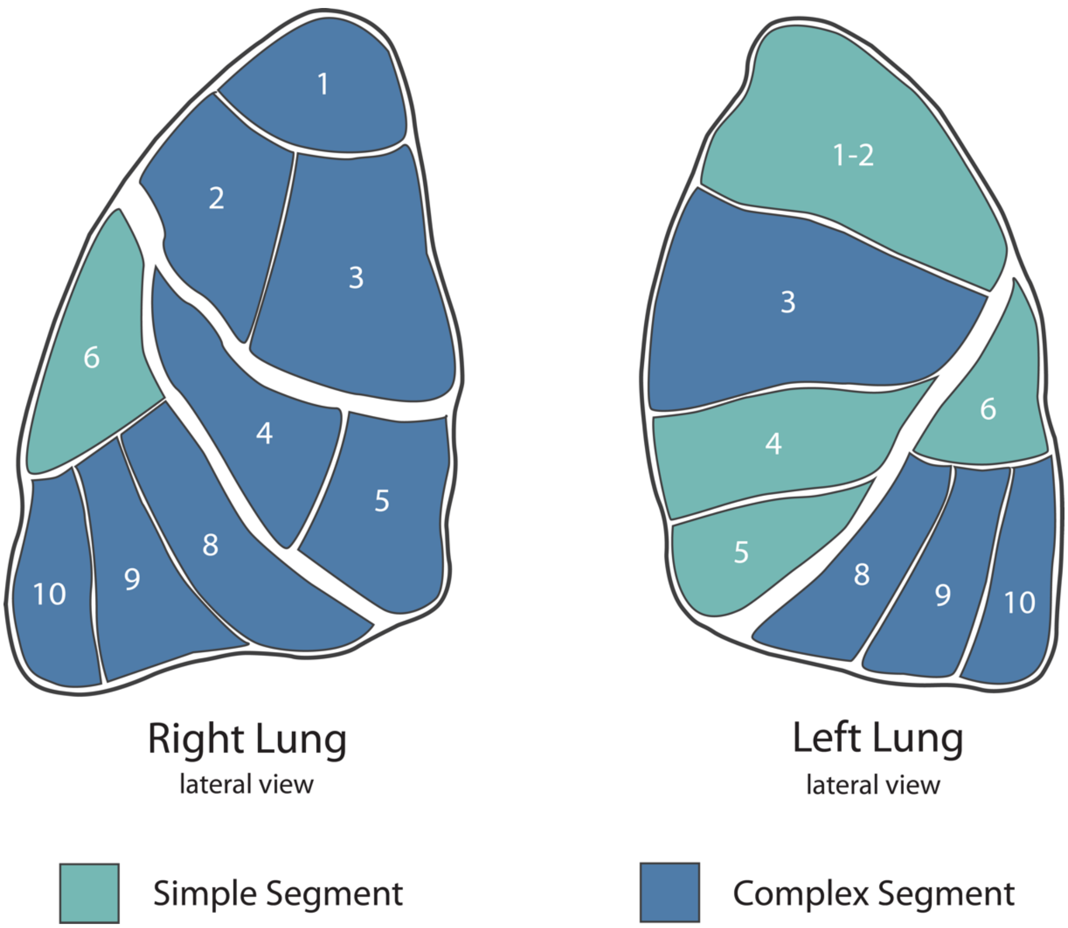
APPENDICES

Appendix 1. Definition of Simple and Complex Segments



Appendix 2. Characteristics of Included Participant

Characteristics of Included Participants				
N = 177, unless otherwise stated	Total N = 177	ICG N = 106	Non-ICG N = 71	p-value
Demographics				
Age in years, mean (SD)	67.02 (8.58)	67.81 (8.58)	65.83 (8.50)	0.133
Male, n (%)	76 (42.94)	43 (40.57)	33 (46.48)	0.444
BMI in Kg/m^2, mean (SD)	28.71 (6.71)	28.36 (6.29)	29.23 (7.31)	0.396
Smoking Status, n (%)				
Ex-smoker	95 (53.67)	60 (56.60)	35 (49.30)	
Current Smoker	51 (28.81)	27 (25.47)	24 (33.80)	0.476
Never Smoked	31 (17.51)	19 (17.9)	12 (16.90)	
% Predicted FEV, mean (SD); N=171	87.06 (20.24)	87.89 (20.66)	85.78 (19.65)	0.506
% Predicted DLCO, mean (SD); N=165	76.96 (19.12)	76.99 (20.03)	76.92 (17.75)	0.982
Comorbidity, n (%)	167 (94.35)	100 (94.34)	67 (94.36)	1.00
Emphysema, n (%)	3 (1.69)	3 (2.83)	0 (0.00)	0.275
COPD, n (%)	53 (29.94)	32 (30.19)	21 (29.58)	1.00
Diabetes, n (%)	40 (22.60)	22 (20.75)	18 (25.35)	0.583
Disease Information				
Previous Cancer, n (%)	81 (45.76)	47 (44.34)	34 (47.89)	0.648
Disease Type, n (%); N=174	N = 174	N = 104	N = 70	0.389
Malignant	134 (77.01)	82 (78.85)	52 (74.29)	
Squamous	18 (10.34)	8 (7.69)	10 (14.29)	
Carcinoid	9 (5.17)	4 (3.85)	5 (7.14)	
Adenocarcinoma	98 (56.32)	65 (62.50)	33 (47.14)	0.129
Small cell	1 (0.57)	0 (0.00)	1 (1.43)	
Large cell	1 (0.57)	0 (0.00)	1 (1.43)	
Other	7 (4.02)	5 (4.81)	2 (2.86)	
Benign	16 (9.20)	7 (6.73)	9 (12.86)	
Necrotizing Granuloma	4 (2.30)	1 (0.96)	3 (4.29)	0.295
Other	12 (6.90)	6 (5.77)	6 (8.57)	
Metastasis	24 (13.79)	15 (14.42)	9 (12.86)	
Colon	12 (6.90)	10 (9.62)	2 (2.86)	
Renal	2 (1.15)	1 (0.96)	1 (1.43)	0.069
Other	10 (5.75)	4 (3.85)	6 (8.57)	
Pathological Stage, n (%); N=130	N = 130	N = 79	N = 51	
Stage I	75 (57.69)	51 (64.56)	24 (47.06)	
Stage II	48 (36.92)	24 (30.38)	24 (47.06)	0.064
Stage III-IV	7 (5.38)	4 (5.06)	3 (5.88)	
Tumour Size, mean (SD); N=148	1.70 (1.05)	1.98 (0.77)	2.01 (0.93)	0.799

Abbreviations: ICG, indocyanine green; SD, standard deviation; BMI, body mass index; FEV, forced expiratory volume; DLCO, diffusing capacity of lung for carbon monoxide; COPD, chronic obstructive pulmonary disease

Appendix 3. Surgical details of included Participants

Operative factors compared between ICG and non-ICG Patients

N = 177, unless otherwise stated	Total N = 177	ICG N = 106	Non-ICG N = 71	p-value
Surgical Details				
Operative Time, mean (SD)	127.10 (32.34)	132.34 (29.10)	119.27 (35.44)	**0.008**
Number of lymph nodes sampled, median (IQR)	7.00 (4.00-7.00)	7.00 (5.00-9.00)	6.00 (4.00-8.00)	**0.008**
Complexity, n (%)				
Simple	85 (48.02)	51 (48.11)	34 (47.89)	1.00
Complex	92 (51.98)	55 (51.89)	37 (52.11)	
Primary Lobe undergoing resection, n (%)				
RUL	28 (15.82)	17 (23.94)	11 (10.38)	
RML	3 (1.69)	1 (1.41)	2 (1.89)	
RLL	49 (27.68)	35 (49.30)	14 (13.21)	0.193
LUL	61 (34.46)	31 (43.66)	30 (28.30)	
LLL	35 (19.77)	22 (30.99)	13 (12.26)	
Complications, n (%)	19 (10.73)	11 (15.49)	8 (7.55)	0.158
Conversion, n (%)	19 (10.73)	3 (2.83)	16 (22.54)	
Conversion to Open	18 (10.17)	2 (1.89)	16 (22.54)	**<0.001**
Conversion to VATS	1 (0.56)	1(1.41)	0 (0.00)	
Completion Lobectomy	30 (16.95)	7 (6.60)	23 (32.40)	**<0.001**
Additional lung surgery performed	55 (31.07)	26 (24.53)	29 (40.85)	**0.031**
Peri-Operative Information				
Adverse Events, n (%)	93 (52.54)	54 (50.94)	39 (54.93)	0.596
Length of Stay, median (IQR)	3.00 (2.00-5.00)	3.00 (2.00-5.00)	3.00 (2.00-5.00)	0.494
Blood Loss >25mL, n (%); N=174	107 (61.49)	61 (59.22)	44 (61.97)	0.751
Total Blood Loss*, mean (SD); N = 107	127.67 (113.56)	111.19 (92.69)	151.27 (135.79)	0.093

Abbreviations: ICG, indocyanine green; SD, standard deviation; IQR, interquartile range; RUL, right upper lobe; RML, right middle lobe; RLL, right lower lobe; LUL, left upper lobe; LLL, left lower lobe; VATS, video-assisted thoracoscopic surgery

*Blood loss values were only collected for participants with ≥25 mL of blood loss during surgery. The mean blood loss volume is calculated based only on those individuals.

Appendix 4. Interphase Analysis between Learning Phases

Operative factors of Patients receiving ICG Segmentectomy between Phases

N = 106, unless otherwise stated	Total N = 106	Phase 1 N = 62	Phase 2 N = 44	p-value
Surgical Details				
Operative Time, mean (SD)	132.34 (29.10)	139.35 (26.95)	122.45 (29.43)	**0.003**
Number of lymph nodes sampled, median (IQR); N=104	7.00 (5.00-9.00)	6.00 (4.00-6.00)	8.00 (6.00-8.00)	**0.023**
Complexity, n (%)				
Simple	51 (48.11)	33 (53.23)	18 (40.91)	0.240
Complex	55 (51.89)	29 (46.77)	26 (59.09)	
Primary Lobe undergoing resection, n (%)				
RUL	17 (16.04)	3 (4.84)	14 (31.82)	
RML	1 (0.94)	0 (0.00)	1 (2.27)	
RLL	35 (33.02)	23 (37.10)	12 (27.27)	**0.002**
LUL	31 (29.25)	21 (33.87)	10 (22.73)	
LLL	22 (20.75)	15 (24.19)	7 (15.91)	
Complications, n (%)	8 (7.55)	3 (4.84)	5 (11.36)	0.272
Conversion, n (%)	3 (2.83)	3 (4.84)	0 (0.00)	
Conversion to Open	2 (1.89)	2 (0.32)	0 (0.00)	0.265
Conversion to VATS	1 (0.94)	1 (0.16)	0 (0.00)	
Completion Lobectomy	7 (6.60)	5 (8.06)	2 (4.55)	0.697
Additional lung surgery performed	26 (24.53)	12 (19.35)	14 (31.82)	0.172
Peri-Operative Information				
Adverse Events, n (%)	54 (50.94)	29 (46.77)	25 (56.82)	0.718
Length of Stay, median (IQR)	3.00 (2.00-5.00)	3.00 (2.00-5.00)	3.00 (2.00-5.00)	0.982
Blood Loss >25mL, n (%); N=103	61 (59.22)	20 (33.90)	41 (93.18)	**<0.001**
Total Blood Loss*, mean (SD); N = 61	111.19 (92.69)	127.73 (87.94)	102.32 (95.01)	**0.007**

Abbreviations: SD, standard deviation; IQR, interquartile range; RUL, right upper lobe; RML, right middle lobe; RLL, right lower lobe; LUL, left upper lobe; LLL, left lower lobe; VATS, video-assisted thoracoscopic surgery
*Blood loss values were only collected for participants with ≥25 mL of blood loss during surgery. The mean blood loss volume is calculated based only on those individuals.

Appendix 5. Impact of Segment Complexity on Surgical and Peri-operative factors

Operative Factors of Patients Receiving ICG Segmentectomy based on Complexity

N = 106, unless otherwise stated	Total N = 106	Simple N = 51	Complex N = 55	p-value
Surgical Details				
Operative time, mean (SD)	132.34 (29.10)	121.49 (28.13)	142.4 (26.44)	**<0.001**
Number of lymph nodes sampled, median (IQR); N= 104	7.00 (3.30)	6.00 (4.00-8.00)	8.00 (6.00-10.50)	**0.004**
Complications, n (%)	8 (7.55)	5 (9.80)	3 (5.45)	0.477
Primary Lobe undergoing resection, n (%)				
RUL	17 (16.04)	0 (0.00)	17 (30.91)	
RML	1 (0.94)	1 (1.96)	0 (0.00)	
RLL	35 (33.02)	20 (39.22)	15 (27.27)	**<0.001**
LUL	31 (29.25)	21 (41.18)	10 (18.18)	
LLL	22 (20.75)	9 (17.65)	13 (23.64)	
Conversion, n (%)	3 (2.83)	3 (5.88)	0 (0.00)	
Conversion to Open	2 (1.89)	2 (3.92)	0 (0.00)	0.108
Conversion to VATS	1 (0.94)	1 (1.96)	0 (0.00)	
Completion Lobectomy	7 (6.60)	4 (7.84)	3 (5.45)	0.709
Additional lung surgery performed	26 (24.53)	11 (21.57)	15 (27.27)	0.509
Peri-Operative Information				
Adverse Events, n (%)	54 (50.94)	25 (49.02)	29 (2.73)	1.00
Length of Stay, median (IQR)	3.00 (2.00-5.00)	3.00 (2.00-5.00)	3.00 (2.00-5.00)	0.886
Blood Loss >25mL, (n) %; N = 103	61 (59.22)	27 (56.25)	34 (61.82)	0.688
Total Blood Loss*, mean (SD); N = 61	68.01 (90.48)	52.71 (68.42)	81.36 (104.88)	0.109

Abbreviations: SD, standard deviation; IQR, interquartile range; RUL, right upper lobe; RML, right middle lobe; RLL, right lower lobe; LUL, left upper lobe; LLL, left lower lobe; VATS, video-assisted thoracoscopic surgery
*Blood loss values were only collected for participants with ≥25 mL of blood loss during surgery. The mean blood loss volume is calculated based only on those individuals.