Original Article

Agreement between observed and predicted postoperative forced expiratory volume in one second, forced vital capacity, and diffusing capacity for carbon monoxide after anatomic lung resection

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Background: Despite its importance in clinical practice, clinical guideline pathway selection and as an outcome in clinical trials, little work has been undertaken to understand the agreement between expected lung function loss and actual observed values. This is particular pertinent in view of the unexpected findings of JCOG 0802 and CALBG 140503 demonstrating no clinically meaningful difference in lung function loss between the sub-lobar resection and lobectomy arm.

Methods: We performed a retrospective analysis on preoperative and postoperative forced expiratory volume in one second (FEV1), forced vital capacity (FVC) and diffusing capacity for carbon monoxide (DL_{CO}) collated from 158 patients who underwent anatomical lung resection between January 2013 to July 2023. Patient's true preoperative and postoperative lung function was obtained via formal lung function testing while predicted postoperative lung function was derived using the 20-segment counting method. Longitudinal postoperative lung function analysis demonstrated sufficient stability over time. A formal testing of agreement between predicted and true postoperative lung function was undertaken using the Bland and Altman method and graphically demonstrated using scatter plots. We defined a deviation of more than 5% as a clinically minimally important difference.

Results: Scatter plots for effort-dependent measures suggested the tendency for underprediction (observed values were higher than predicted) for FEV1 and FVC but good agreement for DL_{CO}. Formal agreement confirmed mean difference for FEV1 was −9.84% [95% confidence interval (CI): −39.33% to 19.65%], FVC −11.39% (95% CI: −50.14% to 27.36%) and DL_{CO} −4.83% (95% CI: −25.59% to 15.92%).

Conclusions: Our study demonstrated that effort-dependent parameters of lung function including FEV1 and FVC tends to overestimate the amount of lung function loss after anatomic lung resection, clinicians should be cautious in using these measures to determine suitability of surgery based on current established guidelines. However, independent measures such as DL_{CO} demonstrate good agreement suggesting that predicted lung tissue loss is consistent with a 20-segment lung model.

Keywords: Segment-counting; postoperative lung function prediction; lobectomy; segmentectomy; video-assisted thoracoscopic surgery (VATS)

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Introduction

The recently published results of JCOG 0802 and CALBG 140503 demonstrated no clinically meaningful difference in lung function loss between patients randomised to sub-lobar resection or lobectomy for lung cancer (1,2). The findings were both surprising and counterintuitive given the inclusion criteria of small lesions less than 2 cm and led many surgeons to question if current assessment of postoperative lung function is accurate and pertinent.

Prediction of postoperative lung function is most commonly achieved with segment counting with the assumption that each segment contributes 5% of lung function. It is the principal method recommended in surgical guidelines worldwide (3,4) and currently how most surgeons predict anticipated losses in lung function for patients who are considering surgery for lung cancer.

Despite its importance, little work has been undertaken on the agreement between expected lung function loss and actual observed values. There is currently no information with regards to the validation of segment counting between effort-dependent measures such as forced expiratory volume in one second (FEV1) and forced vital capacity (FVC) (as reported by trials) and effort independent measures such as transfer factor or diffusing capacity for carbon monoxide (DL_{CO}). Previous studies have reported conflicting evidence in relation to the residual lung function preservation benefits of segmentectomy in comparison to lobectomy (5,6). Possible hypothesis includes variation of lung function at different test time intervals and differing degrees of compensation by amount of resection (7).

In this study, we collated lung function study results before (closest to surgery) and after lung resection surgery (furthest from index surgery) with the aim to examine the agreement between predicted postoperative lung function through segment counting on both effort-dependent and -independent measures of lung function. Our aim is to determine the agreement of postoperative lung function prediction for patients through segment counting to inform surgeon and patient decision-making processes and future guidelines. We present this article in accordance with the STROBE reporting checklist (available at https://jtd.amegroups.com/article/view/10.21037/jtd-23-1390/rc).

Highlight box

Key findings

- Predicted effort-dependent parameters of lung function including forced expiratory volume in one second (FEV1) and forced vital capacity (FVC) tend to overestimate the amount of lung function loss after anatomic lung resection. Independent measures such as diffusing capacity for carbon monoxide (DL_{CO}) demonstrate good agreement suggesting that predicted lung tissue loss is consistent with 20-segment lung model.

What is known and what is new?

- There is no literature on the validation of segment counting between effort-dependent measures such as FEV1 and FVC (as reported by JCOG 0802 and CALBG 140503) and effort independent measures such as DL_{CO}. This study aims to add upon our understanding.
- Conflicting evidence exists in relation to the residual lung function preservation benefits of segmentectomy in comparison to lobectomy. Hypothesis includes different lung function test time intervals and differing degrees of compensation by the amount of resection.

What is the implication and what should change now?

- Clinicians should be aware of our findings and adopt a cautious approach when using these measures to determine patient suitability of surgery based on current established guidelines.

Methods

Participants

We performed a retrospective analysis of prospectively collected data from patients undergoing lung surgery at a tertiary academic hospital. We included all patients undergoing lung resection at the Royal Brompton and Harefield hospitals and excluded those not receiving anatomic lung resection (e.g., wedge resections) or if there was no paired lung function testing both before and after surgery. Anatomical lung resections were performed using stapler-based (fissure and segmental plane) approaches or open blunt dissection of the segmental planes specific to the operating surgeon.

All formal lung function test was performed according to the United Kingdom Association for Respiratory Technology & Physiology guidelines. Patient results were reported as percentage predicted values adjusted for gender, age, height and weight and obtained from existing hospital electronic records (T.C.A.).

We used a 20-segment model (ten segments for each lung) with each segment contributing to 5% of lung function. Segment counts were assigned as follows: right upper lobe [3], middle lobe [2], left or right lower lobe [5], left upper division/tri-segmentectomy [3], left lingula [2] and left upper lobe [5]. The reason for a 20-segment model was because of lack of consensus on how nine segments are allocated in the left lung (either left upper division having two segments or left lower lobe having four segments).

The predicted postoperative values for FVC, FEV1 and DL_{CO} were calculated using the following formula: predicted postoperative value = preoperative value × (20 – the number of resected segments)/20.

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). Individual patient consent and the National Health Service (NHS) Research Ethics Committee (REC) review for this retrospective analysis were waived.

Statistical analysis

We plotted longitudinal plots for individual patients' lung function results of FEV1, FVC and DL_{CO} to determine trajectory with time (Figures S1-S3) to determine if lung function parameters were sufficiently stable (to ascertain the need to standardise the follow up time if there were any important variations in lung function) in the presence of multiple lung function tests.

Performance was assessed visually using scatter plots and formal testing of agreement undertaken using Bland and Altman methods (8). We defined a deviation of more than 5% as a clinically minimally important difference (corresponding to the contribution of one segment) and statistical analyses was undertaken (Eric Lim) using R version 4.3.1 (9).

Table 1 Baseline characteristics

Patient characteristics	Values
Age (years), mean [SD]	65 [11]
Procedure, n [%]	
Right upper lobectomy	116 [69]
Right middle lobectomy	18 [11]
Right lower lobectomy	35 [21]
Left upper lobectomy	54 [36]
Left upper division segmentectomy	29 [19]
Left lingula segmentectomy	6 [4]
Left lower lobectomy	60 [40]

SD, standard deviation.

Results

Between January 2013 to July 2023, we obtained lung function results from 1,174 patients and removed records from 1,016 patients who did not fit our inclusion/exclusion criteria leaving 158 patients for analysis. The baseline characteristics are presented in *Table 1*.

Post operative longitudinal lung function plots (Figures S1-S3) demonstrated sufficient stability with time and therefore preoperative lung function results were selected the time closest before surgery and (based on longitudinal plots) postoperative lung function was defined as the longest time from surgery.

Scatter plots for effort-dependent measures suggested the tendency for underprediction (observed values were higher than predicted) for FEV1 and FVC but good agreement for DL_{CO} (*Figure 1*). Formal agreement confirmed mean difference for FEV1 was −9.84% [95% confidence interval (CI): −39.33% to 19.65%], FVC −11.39% (95% CI: −50.14% to 27.36%) and DL_{CO} −4.83% (95% CI: −25.59% to 15.92%) as demonstrated in *Figure 2*.

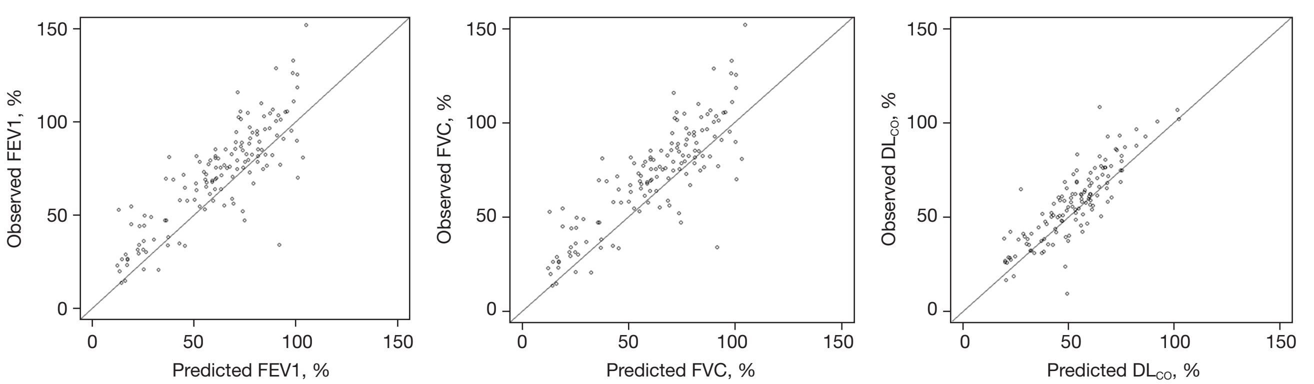

Figure 1 Scatter plots graphically representing the agreement between observed and predicted FEV1, FVC and DL_{CO}. FEV1, forced expiratory volume in one second; FVC, forced vital capacity; DL_{CO}, diffusing capacity for carbon monoxide.

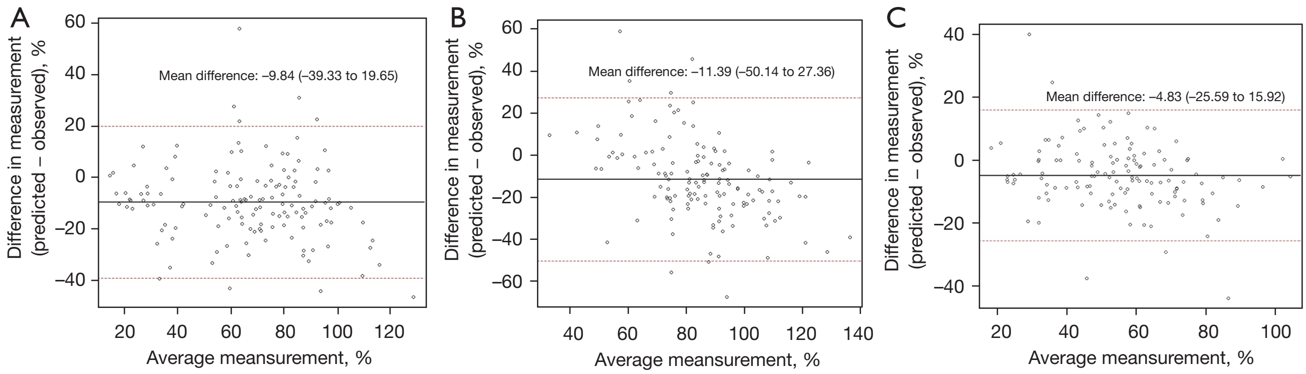

Figure 2 The Bland and Altman plots for FEV1 (A), FVC (B) and DL_{CO} (C). Formal agreement confirmed mean difference for FEV1 was −9.84% (95% CI: −39.33% to 19.65%), FVC −11.39% (95% CI: −50.14% to 27.36%) and DL_{CO} −4.83% (95% CI: −25.59% to 15.92%). FEV1, forced expiratory volume in one second; FVC, forced vital capacity; DL_{CO}, diffusing capacity for carbon monoxide; CI, confidence interval.

Discussion

The results of our study suggested that current methods for prediction of postoperative lung function underestimates the observed values after surgery, reflecting the results reported by other groups (10). For effort-dependent parameters (FEV1 and FVC) the underestimation was considerable of approximately 10% (equivalent of two segments) but there was good agreement with effort independent measures of lung function (DL_{CO}) which was within the 5% of our predefined clinically important threshold. It also validates that a 20-segment model has good agreement with actual amount of (predicted) functional loss from lung resection.

Effort-dependent measures of lung function

There are several plausible considerations as to why postoperative effort-dependent measures of FEV1 and FVC (the two most commonly used estimates in clinical trials as spirometry is easily accessible) are not reliable. We do know however it is not due to lung "recovery" as postulated by some surgeons to explain the higher-than-expected lung function results for JCOG 0802 (1), because the DL_{CO} estimates were very close to that predicted/expected from the amount of lung tissue lost. More plausible explanation might include better technique or efforts after surgery in patients who recovered from surgery (with additional experience of lung function testing) or the possibility that a smaller intrathoracic volume can lead to better diaphragmatic excursion and hence FEV1 and FVC as observed in lung volume reduction surgery (11).

The differences in FEV1 and FVC were clinically significantly higher (better) than expected, and this has important clinical implications. Surgeons often estimate that the amount of lung function loss is directly proportional to the amount of lung tissue resected and the result of our work suggests that this is not accurate. The variation between predicted and observed was considerable of approximately 10% with very wide confidence intervals.

Effort independent measures of lung function

When postoperative predicted lung function was estimated with diffusion capacity for carbon monoxide, the estimated and observed were very close (within 5%, or one segment) leading us to infer that (I) it is a better measure of lung function loss as it is not nearly as dependent on technique and (II) that the 20-segment model for lung function holds true.

Clinical implications

It is unlikely that variation between expected and observed differences in FEV1 and FVC could account for the lack of a difference between segmentectomy and lobectomy in the two large clinical trials [JCOG 0802 (1) and CALGB 140503 (2)]. This is because the degree of error would be expected to be the same on both sides of the randomisation arms. The more likely explanation would be that the amount of lung tissue resected in the sublobar arms would be similar to "lobectomy" to achieve cancer clearance as the 2 cm lesions do not usually sit nicely within the centre of one segment or peripherally to allow a wedge with minimal tissue clearance (as expected when the trials were designed).

Also, the concept of a lobectomy is often misinterpreted as a larger resection given left upper division segmentectomy is the same amount of tissue as right upper lobectomy and left lingula segmentectomy is the same amount of tissue as a right middle lobectomy.

Our results suggest that when consenting patients in clinic prior to lung resection, it is no longer accurate to simply estimate the amount of lung tissue loss if FEV1 is used as a yardstick measure, as it overestimates postoperative losses, and prohibits patients proceeding to surgery or alters the extent of resection recommended on inaccurate measures (12). Future clinical guidelines also need to be aware of our findings to allow for better recommendations for both surgeons and patients. For example, the use of 40% postoperative predicted value is often used as a yardstick for patient selection for lung resection (12) and our results suggest that on average the actual values are expected to be approximately 10% higher.

Limitations

The widespread use of postoperative estimation of lung function seems academic, as it overestimates lung function losses, an outcome that needs to be interpreted by patients rather than doctors or guidelines experts as stated in the 2010 British guidelines (3). For example, patients may accept much lower values of "predicted" lung function losses and choose surgery over non-surgical options. Ultimately, what we need is better measures of functional loss rather than abstract concepts of predicted postoperative lung function, and we hope that this will be a focus for future research efforts. Our patient cohort had principally received lobectomy, so we were unable to ascertain any differential effect on segmentectomy alone, but this was not the focus of our study and may be an aspiration for future work (especially in the setting of "complex" and unusual segment combinations). We did not perform comparisons using other alternatives to segment counting, such as functional lung volume measurement nor were we able to analyse the effect of staples versus blunt dissection on intersegmental planes on postoperative lung function test. Furthermore, we did not distinguish between surgical access (video-assisted thoracoscopic surgery or open) based on the assumption that extent of resection would not differ.

Conclusions

Effort-dependent parameters of lung function (spirometry) including FEV1 and FVC tends to overestimate the amount of lung function loss after anatomic lung resection, clinicians should be cautious in using these measures to determine suitability of surgery based on current established guidelines. However, independent measures such as DL_{CO} demonstrate good agreement suggesting that predicted lung tissue loss is consistent with a 20-segment lung model.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://jtd.amegroups.com/article/view/10.21037/jtd-23-1390/rc

Data Sharing Statement: Available at https://jtd.amegroups.com/article/view/10.21037/jtd-23-1390/dss

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jtd.amegroups.com/article/view/10.21037/jtd-23-1390/coif). Eric Lim is the chief investigator of VIOLET (NIHR 13/04/03), MARS 2 (NIHR 15/188/31) and RAMON (NIHR 131306). He is also the founder of My Cancer Companion, Healthcare Companion Ltd. His other financial disclosures include: consulting payment from Beigene, Roche and BMS and the recipient of grants from AstraZeneca, Medela, Johnson and Johnson/Ethicon, Covidien/Medtronic, Takeda, Lily Oncology. P.D.S. is a recipient of personal fees from Vitae Professionals. J.J.L. received the 2023/2024 Society for Cardiothoracic Surgery and AstraZeneca Thoracic Oncology Educational Fellowship Award. The other authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). Individual patient consent and the National Health Service (NHS) Research Ethics Committee (REC) review for this retrospective analysis were waived.

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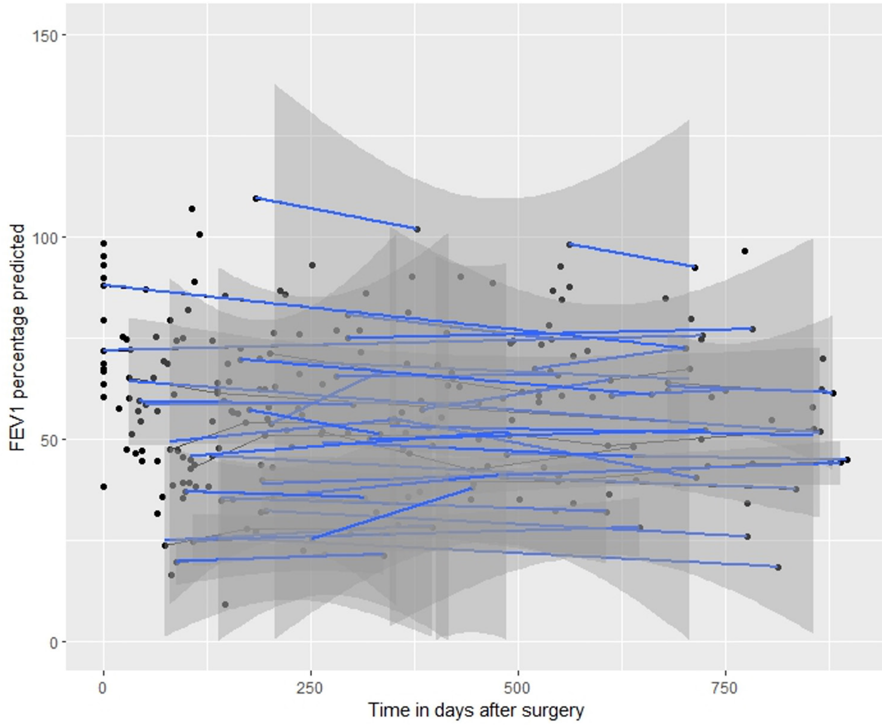

Figure S1 Longitudinal plots for FEV1. FEV1, forced expiratory volume in one second.

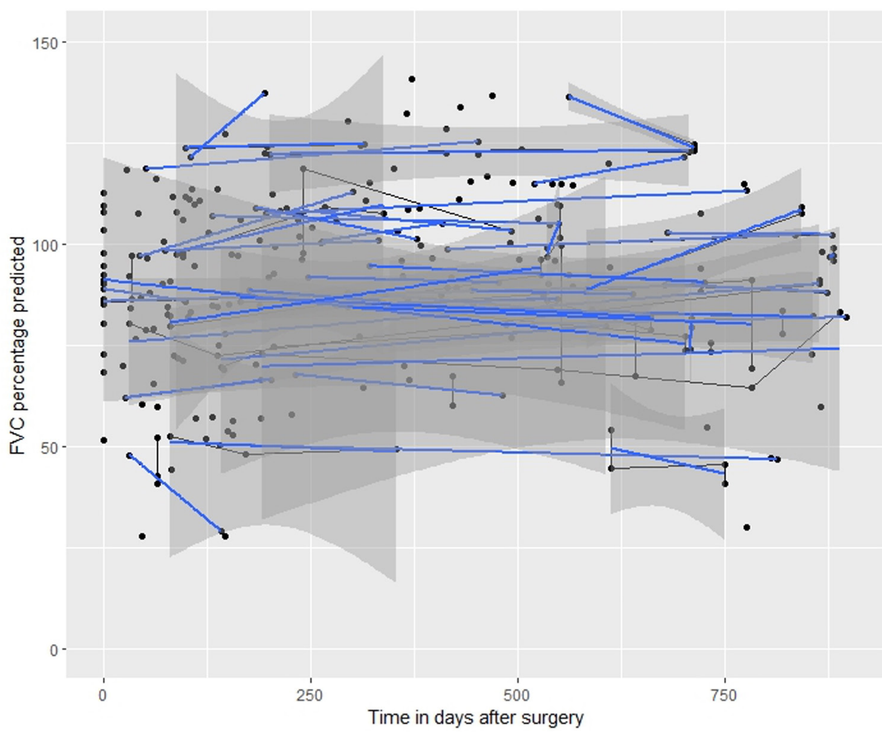

Figure S2 Longitudinal plots for FVC. FVC, forced vital capacity.

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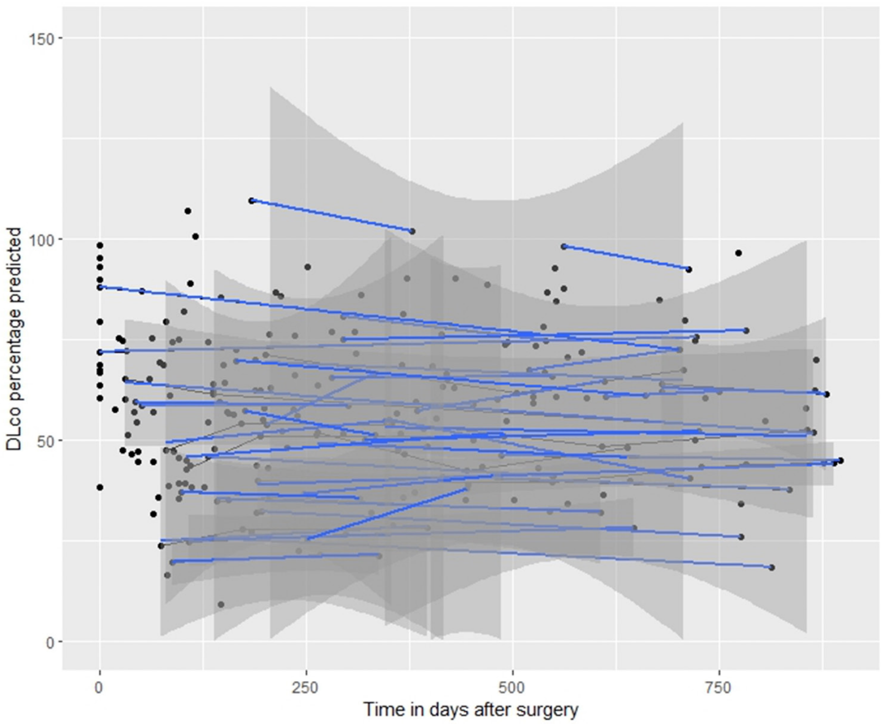

Figure S3 Longitudinal plots for DL_{CO}. DL_{CO}, diffusing capacity for carbon monoxide.

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