



# Recovery from minimally invasive vs. open surgery in kidney cancer patients: Opioid use and workplace absenteeism

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**Purpose:** Does surgical approach (minimally invasive vs. open) and type (radical vs. partial nephrectomy) affects opioid use and workplace absenteeism.

**Materials and Methods:** Retrospective multivariable regression analysis of 2,646 opioid-naïve patients between 18 and 64 undergoing radical or partial nephrectomy via either a minimally invasive vs. open approach for kidney cancer in the United States between 2012 and 2017 drawn from the IBM Watson Health Database was performed. Outcomes included: (1) opioid use in opioid-naïve patients as measured by opioid prescriptions in the post-operative setting at early, intermediate and prolonged time periods and (2) workplace absenteeism after surgery.

**Results:** Patients undergoing minimally invasive surgery had a lower odds of opioid use in the early and intermediate post-operative periods (early: odds ratio [OR], 0.77; 95% confidence interval [CI], 0.62–0.97;  $p=0.02$ , intermediate: OR, 0.60; 95% CI, 0.48–0.75;  $p<0.01$ ), but not in the prolonged setting (prolonged: OR, 1.00; 95% CI, 0.75–1.34;  $p=0.98$ ) and had earlier return to work (minimally invasive vs. open: -10.53 days; 95% CI, -17.79 to -3.26;  $p<0.01$ ). Controlling for approach, patient undergoing partial nephrectomy had lower rates of opioid use across all time periods examined and returned to work earlier than patients undergoing radical nephrectomy (partial vs. radical: -14.41 days; 95% CI, -21.22 to -7.60;  $p<0.01$ ).

**Conclusions:** Patients undergoing various forms of surgery for kidney cancer had lower rates of peri-operative opioid use, fewer days of workplace absenteeism, but no difference in long-term rates of opioid use in patients undergoing minimally invasive as compared to open surgery.

**Keywords:** Absenteeism; Kidney neoplasm; Minimally invasive surgical procedures; Nephrectomy; Opioids

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## INTRODUCTION

There has been an increasing use of minimally invasive surgery for kidney cancer in recent years [1]. While proponents of the approach have argued that better short-term outcomes, including less blood loss and shorter operating time, justify its use [2], others have emphasized that marketing and patient demand have driven its adoption rather than real benefits. Moreover, lack of clear evidence regarding long-term outcomes and high costs of acquisition and maintenance, especially of the robotic platform, have further raised controversy about its use [3]. While prior studies comparing minimally invasive with open surgery have focused on short-term clinical outcomes [4], less is known about longer-term recovery measures that may be important to patients and their care providers.

One important long-term surgical quality measure relates to opioid use in the post-operative setting. Opioid use or lack thereof may serve as a proxy for recovery from surgery and return to normalcy. Opioid use in the post-operative setting is of concern given the potential for misuse and the current epidemic in the United States. Data have shown that the use of opioids around the time of surgery may be an entry point for further opioid use disorder [5]; however, fewer studies have looked at opioid use outside of the immediate post-operative setting, particularly in the setting of urologic procedures [6,7]. While opioid-use and prescribing patterns have traditionally been viewed as a US-centric issue, opioid use and misuse is rising in other developed countries and the US experience may serve as a harbinger for other countries [8]. Another important long-term quality measure is workplace absenteeism. Data from a previous study showed that minimally invasive surgery is associated with fewer days of missed work for a variety of procedures [9]. In theory, if patients returned to work earlier after minimally invasive surgery, the economic benefit of returning to their preoperative state could potentially offset any increased costs of minimally invasive surgery.

To better understand differences in long-term recovery measures between minimally invasive and open kidney surgery, we sought to investigate opioid use and workplace absenteeism in patients undergoing partial and radical nephrectomy for kidney cancer. We hypothesized that patients undergoing a minimally invasive approach with smaller incisions and less immediate perioperative pain, would have less of an opioid requirement and fewer absent days from work.

## MATERIALS AND METHODS

### 1. Data source

We used the IBM Watson Health (formerly Truven Health Analytics) MarketScan<sup>®</sup> Commercial Claims and Encounters Database (IBM, Armonk, NY, USA). From 2012 to 2017, the database contains healthcare claims of approximately two million enrollees. It includes distinct information regarding care in inpatient, outpatient, and emergency department settings, as well as data on outpatient prescription drugs of employees and their dependents who are covered annually under a variety of health plans offered by medium or large-sized firms. Unique patient identifiers allow linkage to another MarketScan<sup>®</sup> database: The Health and Productivity Management Database [10], which contains medical and pharmacy data of a subset of employees in the commercial database based on claims for short-term and long-term disability, medical claims and outpatient drug data. Given that the database only captures prescriptions filled at outpatient pharmacies, inpatient opioid prescriptions were not included in the study. Pharmacy claims data contain the fill date, the supplied quantity, and number of days supplied.

### 2. Study population

We included individuals aged 18 to 64 who underwent minimally invasive vs. open radical or partial nephrectomy for kidney cancer according to the International Classification of Diseases, Ninth Edition (ICD-9) and Tenth Edition (ICD-10; starting in October 1, 2015) along with Current Procedural Terminology (CPT) codes (see Supplementary Table 1). Older patients were not included in this analysis as they were Medicare eligible and not represented in this database. If there were multiple claims for a given surgery, the earliest date was considered as the index surgical date. We excluded those who lacked 12 months of continuous insurance coverage in the same plan pre- and post-index date or if they had incomplete demographic data.

We then selected two cohorts to further analyze long-term recovery from minimally invasive vs. open kidney surgery. For the first cohort (n=2,646), we selected opioid-naive individuals, defined as patients with no opioid prescription within 1 year to 31 days before surgery and with no history of opioid abuse (ICD-9 codes 304.00–304.03, 305.50–305.53; ICD-10 codes F111x, F112x). For the second cohort (n=592), we selected individuals with absenteeism data, which was only available for employees of self-insured firms between 2012 and 2016.

### 3. Outcomes

We investigated two outcome measures of interest: first, we examined filled opioid prescriptions, which we used as a proxy for opioid use, over three time periods: early, intermediate and prolonged. Early was defined a prescription filled on days 0 to 14, intermediate as prescriptions filled between 15 to 90 days and prolonged opioid prescriptions, defined as prescriptions filled between 91 to 180 days from surgery in patients who had also filled at least one prescription within the early time period—0 day to 2 weeks after surgery—as previously described [5]. Second, we evaluated workplace absenteeism, defined as the total number of days absent from work in the perioperative and postoperative period. We defined three discrete time periods relative to the index surgical date—baseline (-380 to -15 days), perioperative (-14 to +28 days), and postoperative (+29 days to +352 days)—as previously described [9]. The number of days absent was converted from hours and calculated for each time period by summing days absent from work due to vacation, sick leave, and short-term disability.

### 4. Covariates

The following covariates were included: age, sex, Elixhauser comorbidity score, US geographic region, urban vs. rural residence, and health plan type (less restrictive vs. more restrictive). For the opioid analysis, we also accounted for risk factors for chronic opioid abuse [11]. Specifically, we accounted for risk factors of depression, substance abuse, and other mental health disorders that occurred within 1 year to 31 days before surgery (see Supplementary Table 2).

### 5. Statistical analyses

Means and proportions were reported for continuous and categorical variables, respectively. To assess differences between the groups we used the t-test for continuous variables and the chi-square test for categorical variables. To assess for the effects of minimally invasive surgery on opioid prescriptions and workplace absenteeism, we created a multivariable model that included pertinent covariates including: age, sex, comorbidities, urban vs. rural setting, geographic region, health plan type, mental health disorders (for opioid analysis) and type of surgery (partial vs. radical). The interaction term of type of surgery (partial vs. radical) and approach (minimally invasive vs. open) was first included in the model. If the interaction term was statistically significant, the results were interpreted with the interaction effect. If the interaction term was not significant, it was removed from the model, and only main effects of type of surgery (partial vs. radical) and approach (minimally invasive vs.

open) was interpreted.

All tests were two-sided and p-values <0.05 were considered significant. Statistical analyses were performed using SAS 9.4 (SAS Institute Inc; Cary, NC, USA). An Institutional Review Board waiver was obtained from Brigham and Women's Hospital (Boston, MA, USA) before conducting the study.

## RESULTS

### 1. Baseline characteristics: minimally invasive vs. open approach

A total of 2,646 patients who underwent either a minimally invasive or open partial or radical nephrectomy were identified in the cohort examining opioid-use post-operatively and 592 patients in the absenteeism cohort were identified as having complete data on workplace participation undergoing the same surgeries and approaches. Both opioid and absenteeism groups had similar rates of use of a minimally invasive approach (opioid: 1,830, 69.16%; absenteeism: 404, 68.24%) and both groups had similar rates of partial and radical nephrectomies (opioid: 49.02% vs. 50.98%; absenteeism: 51.01% vs. 48.99%).

Significant differences within the opioid-naïve cohort were appreciated for baseline characteristics. Specifically, patients with 0 or 1 comorbidities (34.59% vs. 29.78%,  $p=0.02$ ), a less restrictive health plan (68.80% vs. 64.09%,  $p=0.02$ ) and undergoing a partial nephrectomy (51.31% vs. 43.87%,  $p<0.01$ ) were more likely to undergo a minimally invasive vs. open approach (Table 1). Furthermore, rates of post-operative opioid use were noted to be lower in the minimally invasive vs. open cohort in the early (80.55% vs. 84.31%,  $p=0.02$ ) and intermediate time period (126.2% vs. 202.2%,  $p<0.01$ ), however no difference was noted in the prolonged setting (8.85% vs. 9.31%,  $p=0.70$ , Fig. 1, Table 1). In the absenteeism cohort, no significant differences between the minimally invasive and open surgical cohorts across baseline characteristics examined (Table 2).

### 2. Multivariable adjusted analysis: opioid prescriptions and absenteeism

Adjusting for all covariates, we created models to examine opioid use and workplace absenteeism in patients undergoing minimally invasive vs. open partial or radical nephrectomy for kidney cancer (Tables 3, 4). No interaction term was significant for all models. Thus, the interaction term was removed from the models.

After adjusting for all covariates and type of surgery (Table 3), the odds of receiving opioid prescriptions in the early and intermediate time period was significantly lower

**Table 1.** Baseline characteristics of 2,646 opioid-naive patients within the MarketScan® database from 2012–2017

Characteristic	Minimally invasive (n=1,830, 69.16%)	Open (n=816, 30.83%)	p-value
Age (y)	53.82 (7.84)	53.78 (7.86)	0.90
Group			0.74
18–34	45 (2.46)	20 (2.45)	
35–44	180 (9.84)	84 (10.29)	
45–54	612 (33.44)	255 (31.25)	
55–64	993 (54.26)	457 (56.00)	
Elixhauser comorbidity score			0.02*
0	241 (13.17)	81 (9.93)	
1	392 (21.42)	162 (19.85)	
≥2	1,197 (65.41)	573 (70.22)	
Geographic region			<0.01*
Northeast	454 (24.81)	159 (19.49)	
North Central	417 (22.79)	161 (19.73)	
South	706 (38.58)	374 (45.83)	
West	243 (13.28)	111 (13.60)	
Unknown	10 (0.55)	11 (1.35)	
Residence			0.25
Rural	269 (14.70)	134 (16.42)	
Urban	1,561 (85.30)	682 (83.58)	
Health plan type			0.02*
Less restrictive	1,259 (68.80)	523 (64.09)	
More restrictive	571 (31.20)	293 (35.91)	
Sex			0.96
Male	1,142 (62.40)	510 (62.50)	
Female	688 (37.60)	306 (37.50)	
Risk factors			
Depression	130 (7.10)	53 (6.50)	0.57
Substance abuse	133 (7.27)	62 (7.60)	0.76
Other mental health disorders			0.97
Yes	88 (4.81)	39 (4.78)	
No	1,742 (95.19)	777 (95.22)	
Type of surgery			<0.01*
Partial	939 (51.31)	358 (43.87)	
Radical	891 (48.69)	458 (56.13)	
Opioid prescriptions			
Early (0 to 14)	1,474 (80.55)	688 (84.31)	0.02*
Intermediate (15 to 90)	231 (12.62)	165 (20.22)	<0.01*
Prolonged (91 to 180)	162 (8.85)	76 (9.31)	0.70

Values are presented as mean (standard deviation) or number (%).

\*Represents significance at p<0.05.

in patients who underwent a minimally invasive approach (early: odds ratio [OR], 0.77; 95% confidence interval [CI], 0.62–0.97; p=0.02, intermediate: OR, 0.60; 95% CI, 0.48–0.75; p<0.01), however there was no difference in the prolonged time period (prolonged: OR, 1.00; 95% CI, 0.75–1.34; p=0.98). Using the same model, but examining by type of surgery (partial vs. radical nephrectomy), the odds of receiving opioid prescriptions was lower in the early period (OR, 0.67; 95% CI,

0.55–0.82; p<0.01), intermediate (OR, 0.70; 95% CI, 0.56–0.88; p<0.01) and prolonged time period (OR, 0.75; 95% CI, 0.57–0.98; p=0.04).

Absenteeism was examined by surgical approach and type of surgery (Table 4). Patients who underwent a minimally invasive approach experienced approximately 10 fewer days absent from work than patients who underwent an open approach (minimally invasive vs. open: -10.53 days; 95%

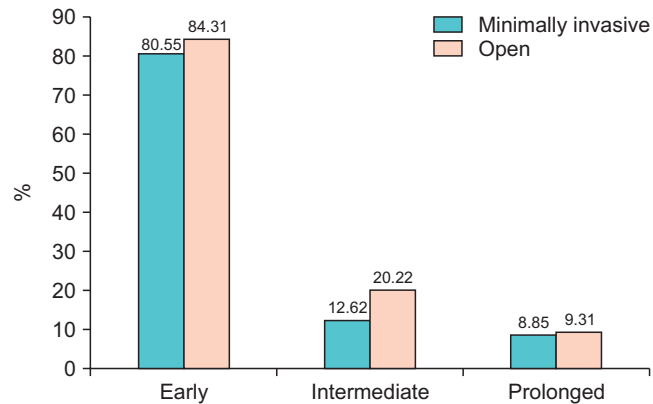
CI, -17.79 to -3.26;  $p < 0.01$ ). Independent of approach, patients who underwent a partial nephrectomy spent fewer days absent from work compared to patients who underwent radical nephrectomy (partial vs. radical: -14.41 days; 95% CI, -21.22

to -7.60;  $p < 0.01$ ).

## DISCUSSION

Our study provides a comprehensive examination between the relationship of how surgical approach in kidney surgery affects perioperative opioid use and workplace absenteeism. We found patients undergoing minimally invasive vs. open nephrectomy had lower odds of early and intermediate perioperative opioid use, but no difference in prolonged opioid use (>90 days). The use of minimally invasive surgery was associated with approximately 10 less days of workplace absenteeism. We also found that partial vs. radical nephrectomy was associated with lower odds of opioid use across all three time periods evaluated and approximately 14 fewer days absent from work.

Our findings are important as they demonstrate benefit to the patient in terms of both undergoing a minimally invasive approach and also possible benefit to partial extir-



**Fig. 1.** Percent opioid prescriptions at measured post-operative time periods.

**Table 2.** Baseline characteristics of 592 patients with complete absenteeism data within the MarketScan® database from 2012–2016

Characteristic	Minimally invasive (n=404, 68.24%)	Open (n=188, 31.75%)	p-value
Age (y)	51.93 (8.07)	51.62 (7.76)	0.67
Group			0.51
18–34	14 (3.47)	3 (1.60)	
35–44	55 (13.61)	31 (16.49)	
45–54	158 (39.11)	73 (38.83)	
55–64	177 (43.81)	81 (43.09)	
Elixhauser comorbidity score			0.79
0	58 (14.36)	24 (12.77)	
1	93 (23.02)	41 (21.81)	
≥2	253 (62.62)	123 (65.43)	
Geographic region			0.30
Northeast	72 (17.82)	30 (15.96)	
North Central	115 (28.47)	53 (28.19)	
South	153 (37.87)	84 (44.68)	
West	64 (15.84)	21 (11.17)	
Residence			0.90
Rural	31 (7.67)	15 (7.98)	
Urban	373 (92.33)	173 (92.02)	
Health plan type			0.23
Less restrictive	238 (58.91)	101 (53.72)	
More restrictive	166 (41.09)	87 (46.28)	
Sex			0.86
Male	278 (68.81)	128 (68.09)	
Female	126 (31.19)	60 (31.91)	
Type of surgery			0.16
Partial	214 (52.97)	88 (46.81)	
Radical	190 (47.03)	100 (53.19)	

Values are presented as mean (standard deviation) or number (%).

**Table 3.** Multivariable-adjusted linear regression predicting days of opioid use in patients undergoing minimally invasive vs. open partial or radical nephrectomy for kidney cancer

Variable	Early	p-value	Intermediate	p-value	Prolonged	p-value
Approach						
Open	1 (ref.)	-	1 (ref.)	-	1 (ref.)	-
Minimally invasive	0.77 (0.62 to 0.97)	0.02*	0.60 (0.48 to 0.75)	<0.01*	1.00 (0.75 to 1.34)	0.98
Surgery						
Radical	1 (ref.)	-	1 (ref.)	-	1 (ref.)	-
Partial	0.67 (0.55 to 0.82)	<0.01*	0.70 (0.56 to 0.88)	<0.01*	0.75 (0.57 to 0.98)	0.04*

Values are presented as odds ratio (95% confidence interval).

-, not available.

\*Represents significance at p<0.05.

**Table 4.** Multivariable-adjusted linear regression predicting days absent from work in patients undergoing minimally invasive vs. open partial or radical nephrectomy for kidney cancer

Variable	Difference in days	p-value
Approach		
Open	1 (ref.)	-
Minimally invasive	-10.53 (-17.79 to -3.26)	<0.01*
Surgery		
Radical	1 (ref.)	-
Partial	-14.41 (-21.22 to -7.60)	<0.01*

Values are presented as mean (95% confidence interval).

-, not available.

\*Represents significance at p<0.05.

pation of kidney tissue on both opioid use and fewer days absent from work. While the rapid adoption of minimally invasive surgery, including robotic surgery, in urology and other surgical specialities over the past decade has been primarily based on the benefits of short-term perioperative outcomes [12], including decreased blood loss, length of stay and decreased inflammatory response, our study suggests there may be additional benefits to the use of minimally invasive surgery. Similarly, while partial nephrectomy has largely been justified to preserve kidney function, enhanced recovery with decreased opioid use and quicker return to work after surgery may be an additional benefit, however in the absence of clinicopathologic data, our results should be interpreted with caution.

A number of factors may be responsible for the trends we observed with respect to postoperative opioid use after kidney surgery. Intrinsic differences between open and minimally invasive surgery could explain the variation in postoperative opioid usage. The larger incisions of and potential extent of disease addressed by open approaches may result in more pain. Our findings echo earlier investigations that demonstrate that minimally invasive surgery is associated with decreased opioid use in the perioperative period [13,14].

With regards to nephrectomy, past literature has generally found that those undergoing laparoscopic nephrectomy have lower acute postoperative pain [15] and need for analgesia [16], although such conclusion are not uniform [17,18]. The finding that a minimally invasive surgical approach reduces early and intermediate perioperative opioid use is meaningful, as decreased opioid use is likely an important contributing factor for enhanced return to normalcy and improved quality of life after surgery.

Whether the higher pain burden of more invasive approaches translates into long-term post-operative opioid use is less clear. One study looking at patients who underwent open or laparoscopic nephrectomy reported similar levels of pain at 2 and 6 months postoperatively [17], while another comparing patients who had received open or laparoscopic radical nephrectomies found no significant difference in pain score at 3 months postoperatively [19]. Thus, our findings of lower postoperative opioid use in the minimally invasive surgery group for the early and intermediate period, but not the prolonged period corroborate these prior results.

Other important factors that could account for this trend in the minimally invasive surgery group may not be captured in our study design, but are worth a discussion nonetheless. Larger initial prescription of opioids after urologic surgery is a risk factor for prolonged opioid use, and evidence suggests that acute postoperative pain may not always correlate well with prolonged opioid use [20]. Thus, despite lower acute postoperative pain in patients receiving minimally invasive surgery, differences in physician prescribing practices between groups could play a role in differences in outcomes. The quantity of opioids initially prescribed could in turn be shaped by physician beliefs about postoperative pain for different approaches, level of patient-reported pain at time of discharge, and different medical practices protocols. Of note, multimodal analgesics have played an increasing role in the management of acute postoperative pain,

although their impact on postoperative opioid use has not been studied [21]. These are important questions and ones that should continue to be investigated.

Patients undergoing minimally invasive nephrectomy were noted to return to work approximately 10 days faster than their open counterparts, a finding that is consistent with similarly published work on workplace absenteeism demonstrating fewer absent days from work following minimally invasive surgery in other fields [9]. This difference in time was not as stark as that found in a prior study examining live donor nephrectomy, where patients undergoing a laparoscopic approach returned to work 5 weeks faster than those undergoing an open approach [22]. Return to work may be a good measure of complete recovery from surgery, as return to work likely represents a multitude of important milestones, including being pain free and off of opioid medication and having enough mobility, stamina and physical strength to perform work duties.

While earlier return to work suggests faster return to pre-operative baseline functional status, there may be additional economic benefits to the patient, employer and society. Patients who are able to return to work more quickly may be able to minimize the financial burden associated with a significant medical disease, be less reliant on short term-disability and reduce workplace disruption with the prolonged absence of an employee, which has been shown to have an impact on cancer costs [23] and there could be benefits to employers as well. Our finding that minimally invasive surgery decreases opioid requirement in the perioperative period may decrease the risk of opioid tolerance, which has been associated with decreased economic activity [24,25]. Prior estimates of nephrectomies have mainly focused on costs from a payer perspective, such as those associated with operating room time, personnel, hospital stay length, and surveillance, without considering decreased opioid use and absenteeism [26].

Our study has several limitations. First, we conducted a retrospective observational study that is susceptible to unmeasured confounding. While we accounted for characteristics that were available in the database, there may be clinical factors and indications for surgical approach, such as tumor staging, that we could not account for that may explain differences between the groups. Second, the information on workplace absenteeism, while large, was only available for a subset of patients and thus our results may not be generalizable to the larger populations. We were also unable to account for the type of work an individual patient performed, which could affect the timeline for return to work, however unclear how this would affect decisions regarding surgical approach.

Third, we could not account for different preoperative, intraoperative, and postoperative management pathways that may explain differences seen between open and minimally invasive surgery, including variations in hospital or surgeons prescribing practices, actual doses of opioid usage, as well as the use of regional anesthetic techniques or adjunct non-opioid pharmacotherapy [27,28]. Despite these limitations, we were able to give insight into a new perspective of differences in long-term recovery measures for minimally invasive surgery for kidney cancer patients and may be important to help guide future clinical work around this topic as well serve as important information for counselling patients.

## CONCLUSIONS

Minimally invasive nephrectomy was associated with decreased odds of opioid use in the early and intermediate perioperative time period and was associated with fewer days absent from work. Similarly, controlling for approach, we found that patients undergoing partial nephrectomy was associated with decreased opioid use across all three time periods and earlier return to work. These findings suggest possible benefits to minimally invasive surgery outside of the traditional outcome metrics.

## CONFLICTS OF INTEREST

Quoc-Dien Trinh reports personal fees from Astellas, Bayer, Janssen, Insightec and Intuitive Surgical. Adam S. Kibel reports consulting fees from Janssen, Merck, Bristol-Myers Squibb, Advantage, Insightec, and Profound. Richard D. Urman reports research funding from Merck and Medtronic and consulting fees from 3M, Mallinckrodt and Sandoz. Prokar Dasgupta is funded by the MRC Centre for Transplantation, NIHR Biomedical Research Centre, Kings College London, The Prostate Cancer Research Centre, The Vattikuti Foundation and The Urology Foundation.

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## AUTHORS' CONTRIBUTIONS

Research conception and design: Stephen W. Reese, Marieke J. Krimphove, Xi Chen, and Maya Marchese. Data acquisition: Marieke J. Krimphove, Xi Chen, and Maya Marchese. Statistical analysis: Xi Chen and Maya Marchese. Data analysis and interpretation: Stephen W. Reese, Marieke J. Krimphove, Xi Chen, and Maya Marchese. Drafting of the manuscript: Stephen W. Reese, Marieke J. Krimphove, and Daniel Pucheril. Critical revision of the manuscript: Eugene Cone, Karl H. Tully, Adam S. Kibel, Wesley Chou, Richard D. Urman, Steven L. Chang, Luis A. Kluth, and Prokar Dasgupta. Obtaining funding: Quoc-Dien Trinh. Administrative, technical, or material support: Luis A. Kluth, Prokar Dasgupta, and Quoc-Dien Trinh. Supervision: Luis A. Kluth, Prokar Dasgupta, and Quoc-Dien Trinh. Approval of the final manuscript: All authors listed.

## SUPPLEMENTARY MATERIALS

Supplementary materials can be found via <https://doi.org/10.4111/icu.20200194>.

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