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Post-surgical opioid prescribing patterns and risk factors for additional opioid prescriptions within one year after non-emergent colorectal surgery

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ABSTRACT

Background: National opioid concerns resulted in review of prescribing patterns following colorectal surgery.
Methods: This retrospective cohort study examined prescribing patterns in elective colorectal surgery at a tertiary academic medical center from January 2012 through December 2014.
Results: Forty percent of 4286 patients received additional opioid prescriptions within the year following colorectal surgery. Multivariable analysis demonstrated that a pre-operative opioid prescriptions within 1 year of surgery (OR 2.91; 95% CI, 1.83–4.60), increasing operative time (OR 1.02; 95% CI, 1.00–1.04), or complications (OR 2.18; 95% CI, 1.38–3.43) was associated with additional opioid prescriptions. The median opioid prescription upon discharge was 225 mg morphine milligram equivalents. Discharge opioid amount was not a risk factor.
Conclusions: Additional opioid prescriptions after surgery occurred in 40% of patients. Pre-operative prescriptions, increasing operative time and complications were associated with additional opioid prescriptions while opioid amount at discharge was not a risk factor.

Introduction

Opioid misuse is a national crisis in the United States and receiving global attention.[1] Given this crisis, healthcare providers are being asked to closely examine prescribing practices which may contribute to misuse.[1] Patients undergoing surgery are at risk for subsequent long-term opioid use.[2–5] While Enhanced Recovery Pathways have reduced inpatient opioid requirements through multimodal care and proactive pain management,[6,7] post-operative prescribing practices are far from optimized with common overprescribing.[8–11]

The current post-operative opioid prescribing patterns are inconsistent and vary widely depending on patient and system factors.[10,11] Guidelines for acute pain recommend that patients be given sufficient opioids for only a short period of time (3–7 days)[12,13] with specific taper-to-off plan.[14] Other opportunities such as preoperative discussions with patients about the side effects of opioids may decrease fill rates on prescriptions post-operatively[15,16]; however, psychosocial stressors and perceptions of pain may raise the level of difficulty when setting standards.[16–19] A recent study of patients in the United States identified the risk of persistent opioid use and misuse increased with each additional opioid prescription.[20]

The goals of this study were to describe the opioid prescribing patterns up to 1 year after colorectal surgery at a tertiary center

Abbreviations: ERP, Enhanced Recovery Pathway; CUC, Chronic Ulcerative Colitis; AHFS, American Hospital Formulary System; MME, Morphine milligram equivalents; IQR, Interquartile range; ORs, Odds ratios; CIs, Confidence intervals; ROC, Receiver operating characteristic; SSI, Surgical Site Infection; PCP, Primary care provider.

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with a standardized perioperative practice. The secondary goal was to characterize the risk factors associated with additional opioid prescriptions prescribed in the year following colorectal surgery.

Methods

This retrospective study took place in a high volume academic tertiary center where approximately 2800 elective colorectal surgeries are performed annually. All patients are cared for through a standardized Enhanced Recovery Pathway (ERP) which is adjusted for individual patients (e.g., not prescribing non-steroidal anti-inflammatory drugs for patients with renal dysfunction)[6] and receive follow up with the institution post-operatively. Inclusion criteria include all patients 18 years or older undergoing inpatient colorectal surgeries from 2012 through 2014. Exclusion criteria included patients who died within the year following surgery or declined participation in retrospective review research studies. The study was approved by the Mayo Clinic Rochester Institutional Review Board.

Patient demographics, reoperation, readmission, and primary surgical endpoints were determined through a census of administrative data. The colorectal American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) dataset, a representative sample of this large cohort, was included to provide additional data elements such as postoperative complications. This data is captured through clinical abstraction and follow up from nurse abstractors as per the ACS-NSQIP standard abstraction methodology.[21] Non-elective surgery patients were excluded. Diagnosis of surgical indication was additionally manually abstracted by clinicians for this subset of patients and grouped into Cancer, Crohn's/Chronic Ulcerative Colitis (CUC), Diverticulitis, Neoplasia and Other.

Medication data from the institution's electronic medical record for each patient up to 1 year before and after the index operation were included in the analysis of administration data. Medications meeting criteria for American Hospital Formulary System (AHFS) class of 'opioid' and 'opioid containing' medications were included in the query. For descriptive statistics, the medications were grouped into short acting, long acting or other by the pharmacist author. The opioid content of each prescription was converted into oral morphine milligram equivalents (MME) to allow for normalized comparisons across different medication and dosage forms.[12,22] For example, a prescription for oxycodone 5 mg immediate release tablets with a dispense quantity of 30 tablets was normalized to 225 MME. A clinical review of the patient's records in those receiving greater than 10 prescriptions in the year or greater than 2000 MME was done to validate data accuracy for extreme numbers. The 'initial dismissal' prescription amount of opioid in MME was defined as prescriptions prescribed between admission and within 1 day after the patient's discharge date. This prescription will be termed "dismissal prescription" in future tables and discussion. Additional opioid prescriptions within 1 year after elective colorectal surgery were defined as any opioid prescriptions provided after the initial dismissal prescription(s). This prescription will be termed "additional prescription" in future tables and discussion. The providers prescribing additional opioid prescriptions were clinically classified into medical and surgical groups. The time in days to first additional prescription was captured and then grouped into weeks for visualization of patients that had not had subsequent surgeries in Fig. 1.

The primary goal of this study was describing patterns of opioid prescriptions within a year prior to surgery up to a year post dismissal from inpatient surgery. Our secondary goal was to understand the multimodal nature of factors leading to additional opioid prescribing for patients undergoing colorectal surgery.

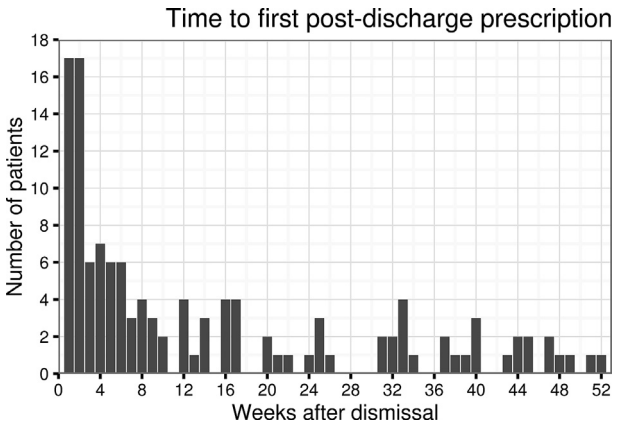

Fig. 1. Time to first post-discharge prescription.

Statistical analysis

Patient characteristic and complications with or without additional opioid prescriptions were summarized as median [interquartile range (IQR)] for continuous variables and frequency (percent) for categorical variables. Comparisons between patient groups were evaluated using chi-square and Mann Whitney U tests as appropriate.

For the subset of patients in the ACS-NSQIP, we excluded patients with emergent surgery, any subsequent surgeries, or any death within the year. Multivariable logistic regression analysis was used to predict additional opioid prescriptions within one year after dismissal. This was summarized with odds ratios (ORs) and 95% confidence intervals (CIs). Opioid amounts were analyzed in increments of 50 MME. Duration of surgery was analyzed using 10 min increments. The factor of primary interest was initial MME amount at the time of dismissal. The discriminative ability of the model was measured with the c-statistic which is similar to the area under the receiver operating characteristic (ROC) curve and ranges from 0.5 to 1.0, with values of 0.5 indicating no discrimination, and 1.0 indicating perfect discrimination. Factors considered in the logistic regression model were age, gender, preoperative opioids at 1 year, operative time (in increments of 10 min), diagnosis of Crohn's/CUC, Cancer, Diverticulitis, Neoplasia or Other, any postoperative complications, any 30 day readmission, or SSI. A selection of factors from univariate analyses was included in the multivariable model to maximize the c-statistic. The statistical analyses were performed using the software R version 3.3.1 and SAS version 9.4. A level of 0.05 was considered statistically significant.

Results

Full cohort

A total of 4286 patients were included for analysis. Nearly half (n = 2058, 48%) of patients in the full cohort had pre-operative prescriptions for opioids in the year prior to elective colorectal surgery, and 686 patients (16%) had received an opioid prescription within 14 days prior to surgery or reported current use. Most patients (n = 3638, 84.9%) were discharged with prescription(s) for opioids, and the median MME prescribed was 225 [IQR 100–600) (Table 1). This corresponds to a prescription of approximately 30 tablets of immediate release oxycodone 5 mg. The opioids prescribed initially on dismissal were short-acting agents 97.7% of the time. Many patients (n = 1664, 39%) received additional opioid

Table 1
Patient demographics and characteristics comparing patients with additional opioid prescriptions with those who did not in each cohort.

	Full Cohort			Institutional ACS NSQIP subset		
	No additional Opioid RX (n = 2622)	Additional Opioid RX (n = 1664)	p-value	No additional Opioid RX (n = 483)	Additional Opioid RX (n = 328)	p-value
Age at surgery, Median [IQR]	57 [42,69]	50 [35,63]	<0.0001[a]	58 [41,69]	52 [35,63]	<0.0001[a]
Gender, No. (%)						
Male	1329 (61)	847 (39)	0.89[b]	222 (58)	161 (42)	0.38[b]
Female	1293 (61)	817 (39)		261 (61)	167 (39)	
Prescribed opioid in year prior to surgery, No. (%)						
Yes	1137 (55)	921 (45)	<0.0001[b]	195 (52)	178 (48)	0.0001[b]
No	1485 (67)	743 (33)		288 (66)	150 (34)	
Prescribed opioid in 14 days prior to surgery, No. (%)						
Yes	330 (48)	356 (52)	<0.0001[b]	54 (44)	69 (56)	0.0001[b]
No	2292 (64)	1308 (36)		429 (62)	259 (38)	
Length of stay (days), Median [IQR]	3 [2,5]	4 [3,6]	<0.0001[a]	3 [2,5]	4 [3,6]	0.0068[a]
Procedure mode, No. (%)						
Lap/Robotic	588 (63)	351 (37)	<0.0001[b]	125 (63)	75 (38)	0.0040[b]
HALS	384 (54)	330 (46)		68 (47)	76 (53)	
Open	1650 (63)	983 (37)		290 (62)	177 (38)	
Surgical duration (minutes), Median [IQR]	141 [95,200]	183 [126,247]	<0.0001[a]	150 [98,215]	190 [133,261]	<0.0001[a]
Reoperation within 30 days, No. (%)						
Yes	80 (35)	152 (66)	<0.0001[b]	12 (27)	32 (73)	<0.0001[b]
No	2542 (63)	1512 (37)		471 (61)	296 (39)	
Readmission to institution within 30 days, No. (%)						
Yes	142 (29)	353 (71)	<0.0001[b]	61 (41)	87 (59)	<0.0001[b]
No	2480 (65)	1311 (35)		422 (64)	241 (36)	
Prescribed opioid upon dismissal, No. (%)						
Yes	2157 (59)	1481 (41)	<0.0001[b]	393 (58)	287 (42)	0.020[b]
No	465 (72)	183 (28)		90 (69)	41 (31)	
Sum of MME upon dismissal, Median [IQR]	225 [75,450]	300 [150,650]	<0.0001[a]	225 [75,480]	369 [150,750]	<0.0001[a]
Sum of MME prescribed within 1 year of surgery, Median [IQR]	225 [75,450]	900 [500,1925]	<0.0001[a]	225 [75,480]	973 [475,1980]	<0.0001[a]

[a] Mann-Whitney *U* test.
[b] Chi-Square.

prescription(s) after the initial prescriptions upon dismissal in the year following surgery. A total of 4974 additional opioid prescriptions were prescribed for 1664 patients. Patients receiving additional prescriptions received a median of 2 (IQR 1–3) prescriptions with a median MME of 484 (IQR 225–1165) each. Of the 4974 additional opioid prescriptions from our institution, 1438 (30%) were from a medical prescriber, 3430 (70%) from a surgical prescriber, and 106 from unknown specialty prescribers (Table 1).

On univariate analysis of the full cohort, younger age, opioid prescriptions in the prior year or within 14 days preceding surgery, duration of surgery, longer length of stay in hospital, re-operation within 30 days, subsequent surgery within the year, readmission, receipt of an opioid prescription at dismissal and amount of initial MME on dismissal were associated with additional opioid prescriptions within the year following colorectal surgery (Table 1).

Subset of patients in ACS NSQIP cohort

A subset of 811 patients (21%) had additional data captured as part of the institution's ACS NSQIP dataset. The characteristics of the NSQIP cohort were similar to that of the full cohort (Table 1). Most (n = 680, 83.8%) patients were discharged with opioid prescriptions with a median MME prescribed of 250 mg (IQR 100–630, range 0–30,000), representing a prescription of 33 tablets of immediate release oxycodone 5 mg. The 811 patients had a total of 975 opioid prescriptions prescribed for patients for dismissal. Some patients received more than one opioid prescription at dismissal. Of these opioid prescriptions at dismissal, 950/975 (97.4%) of prescriptions were for short acting opioids oxycodone, hydromorphone, morphine or tramadol, and 19/975 (3.2%) were for long acting oral agents, patches or other forms of opioids. Univariate analysis demonstrated the same risk factors for additional opioid prescriptions as the full cohort.

Similar to the full cohort, 40% of the 811 patients received additional opioid prescriptions after the initial dismissal prescriptions in the 1 year following surgery. Patients receiving additional prescriptions received a median of 2 (IQR 1–3) prescriptions with a median MME of 555 (IQR 225–1175) for subsequent prescriptions. The time to first additional prescription was 85 days (IQR 24–151). For the patients in the NSQIP subset without subsequent surgeries (n = 574), the time to first additional prescription was 48 days (IQR 14–172). The timing of additional prescriptions was grouped into weeks after surgery and shown in Fig. 1.

Additional risk factors were evaluated using the ACS NSQIP subset of elective colorectal surgery patients. On univariate analysis, a patient's diagnosis was associated with additional prescriptions, with a larger proportion of patients with the diagnosis of Crohn's/CUC receiving additional prescriptions (n = 109, 53%) (Table 2). Of the other diagnosis groups, at most 40% received additional opioid prescriptions in the year following surgery. Patients with any postop complications (n = 257, 31.7%, p = 0.0001), specifically SSI and Sepsis, had higher proportions of additional opioid prescriptions in the year after surgery (Table 3).

A multivariable analysis of the 811 patients with ACS NSQIP data (excluding patients having subsequent surgeries) adjusted for age, gender and diagnosis found that having a pre-operative opioid prescriptions within 1 year of surgery (OR 2.91; 95% CI, 1.83–4.60), increasing operative time (OR 1.02; 95% CI, 1.00–1.04), or any complications (OR 2.18; 95% CI, 1.38–3.43), were associated with additional opioid prescriptions (Table 4). The initial prescribed MME amount was not independently associated with additional prescriptions. The c-statistic for the multivariable model was c = 0.693.

Table 2
Subset of Patient Diagnosis. Groups for institution's ACS-NSQIP: a Comparison of patients with additional opioid prescriptions and those without after dismissal.

	No additional Opioid Prescriptions (n = 483)	Additional Opioid Prescriptions (n = 328)	Total (n = 811)	p-value
Diagnosis, No. (%)				0.0001[a]
Cancer	151 (62)	92 (38)	243	
Crohn's/CUC	95 (47)	109 (53)	204	
Diverticulitis	67 (60)	44 (40)	111	
Neoplasia	32 (78)	9 (22)	41	
Other	138 (65)	74 (35)	212	

[a] Chi-Square.

Discussion

The current study describes opioid prescribing patterns upon dismissal and in the year following colorectal surgery in a high-volume tertiary practice with standardized peri-operative management pathways. The median MME prescribed at discharge was 225 mg, and (40%) of patients had additional opioid prescriptions in the 1 year following elective colorectal surgery. Risk factors for receiving additional opioid prescriptions were having opioid prescriptions in the year prior to surgery, increasing operative time, and any post-operative complications. Initial opioid amount at discharge was not associated with additional opioid prescriptions.

Prescribing patterns

Our findings demonstrate that there is wide variation of opioid prescribing upon discharge after surgery. This is consistent with a new study from parallel work at the institutional level. Thiels et al. found wide variation in prescribing at dismissal.[11] Unique to Colorectal surgery, we found that median prescription MME fell within current CDC guidelines. There is still an opportunity to decrease unnecessary variation or excess prescribing, stressing the need for collaboration across medical, surgical and allied health teams to address pain management. Current CDC guidelines,[12] written with a non-cancer chronic pain focus, suggest that acute pain opioid prescribing be only for those patients where severe pain is expected and to limit duration to a short course of 3 days, rarely up to a week supply. Recent findings show a significant increase of prolonged use with more than 7 day prescription quantities at discharge.[20] Using the proposed calculation of 50 MME/day for 3 days (150 MME) and up to a week supply when needed (350 MME), our median prescribing is within this construct (225–250 MME). Others have reported a similar prescribing range in an opioid naïve population.[23]

However, the large variability in amount prescribed suggests there is great room for improvement. The range at discharge ranged from 0 to 30,000 MME. While some variation is to be expected and encouraged to better reflect the lowest amount for the patients' need, a standardized systematic approach for how to arrive at an appropriate amount has yet to be determined or implemented. The use of short acting agents in nearly 100% of prescriptions is consistent with practice standards for the acute pain settings. In manual review for several patients receiving large amounts, we recognized that coverage for both acute and acute on chronic pain needs was being prescribed on dismissal. This suggests additional collaboration in hand off between surgeons and the patient's primary care provider (PCP) is critical. Nearly a third of patients receive their additional opioid prescriptions from medical (as opposed to surgical) providers. Encouraging patients to work with their PCP to explicitly taper off acute opioid amounts while using the support of other non-pharmacologic and non-opioid options for optimal pain management will be important in returning patients to their baseline or taper off opioids entirely.

We were surprised to find out that in patients only undergoing the index operation, the median time from discharge to their subsequent opioid prescription was 48 days. This suggests that targeted interventions for triage, patient counseling and identification of responsible provider may need to extend beyond the typical timeframe associated with an operation (30 days). Non-surgical pain or issues may also need to be addressed differently in concert with the patient and the patient's primary care provider. With the Morbidity Mortality Weekly Report from the CDC demonstrating that any subsequent prescriptions putting patients at higher risk for longer term use, each prescription and amount prescribed is important.[20] Surgeons will need to work closely with primary care providers on appropriate pain management techniques, opioid stewardship, and appropriate infrastructure for non-pharmacologic and behavioral support teams.

Table 3
Institution's ACS-NSQIP patient subset with complications within 30 days: Comparison of patients with additional opioid prescriptions and those without after dismissal.

	No additional Opioid Prescriptions (n = 483)	Additional Opioid Prescriptions (n = 328)	Total (n = 811)	p-value
Superficial SSI, No. (%)				0.0012[a]
No	469 (61)	302 (39)	771	
Yes	14 (35)	26 (65)	40	
Organ Space SSI, No. (%)				<0.0001[a]
No	474 (61)	301 (39)	775	
Yes	9 (25)	27 (75)	36	
Any Readmission, No. (%)				<0.0001[a]
No	422 (64)	241 (36)	663	
Yes	61 (41)	87 (59)	148	
Any Return to OR, No. (%)				<0.0001[a]
No	465 (62)	290 (38)	755	
Yes	18 (32)	38 (68)	56	
Any Postoperative Complication, No. (%)				<0.0001[a]
No	367 (66)	187 (34)	554	
Yes	116 (45)	141 (55)	257	

SSI=Surgical Site Infection; OR=Operating Room.
[a] Chi-Square.

Table 4
Univariate and multivariable models predicting additional opioid prescriptions in ACS-NSQIP elective colorectal surgery patients excluding subsequent colorectal surgeries within 1 year (n = 576).

Variable	Univariate		Multivariable	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Initial prescribed MME amount (in increments of 50 MME)	1.04 (1.01,1.08)	0.014	1.02 (0.99,1.06)	0.217
Pre-op opioid prescription within 1 year	2.54 (1.68, 3.83)	<0.001	2.91 (1.83, 4.60)	<0.001
Operative time (in 10 min increments)	1.02 (1.00, 1.04)	0.034	1.02 (1.00, 1.04)	0.040
Any complications	2.25 (1.47, 3.43)	<0.001	2.18 (1.38, 3.43)	0.001
Readmission within 30 days	2.49 (1.53, 4.07)	0.003		
SSI	2.34 (1.11, 4.93)	0.025		
Age	1.00 (0.99,1.01)	0.969	1.00 (0.99, 1.02)	0.239
Sex	1.00 (0.53, 1.20)	0.278	0.80 (0.52, 1.22)	0.301
Diagnosis				
	Reference		Reference	
Cancer	1.01 (0.56,1.81)	0.983	0.91 (0.46, 1.80)	0.793
Crohn/CUC	0.93 (0.49, 1.78)	0.839	0.98 (0.49, 1.96)	0.950
Diverticulitis	0.48 (0.16, 1.46)	0.198	0.68 (0.22, 2.14)	0.514
Neoplasia/Other	1.09 (0.66, 1.81)	0.723	1.03 (0.56, 1.85)	0.916

MME = morphine milligram equivalents; NA = not applicable; ACS-NSQIP = American College of Surgeons National Surgical Quality Improvement Program.

Risk factors

We found that having a pre-operative opioid prescription increased the risk of requiring additional opioid prescriptions after surgery. This is consistent with previous studies which found this to be true in patients with opioid exposure in the 30 days prior to surgery.[27] Our study suggests that this window of increased risk extends out much further with 48% of our full cohort having an opioid prescription in the year prior to surgery. This is quite a bit higher than previous studies suggesting that 15–21% of patients use opioids prior to major abdominal surgery.[24] If the window of risk indeed stretches out more than 30 days, we may underestimating how prevalent opioid exposure is in patients undergoing non-emergent surgery. Interestingly, Cron and colleagues have reported that pre-operative opioid use was associated with an increased risk of surgical complications, particularly infectious.[24] If this is indeed true, then better management of pre-operative opioids may not only reduce post-operative opioid use but also improve surgical outcomes.

The association between the duration of surgery and increased post-operative opioid prescriptions likely reflects many factors, some which are modifiable and others which are not. Longer operations are probably associated with more complex operations. How this directly relates to increased opioid risk is not clear. Several studies have linked inpatient and complex procedures are associated with an increased risk of additional opioid use.[3,20]

To our knowledge, this is the first study to use ACS-NSQIP complication data to show a relationship between complications and the risk of additional opioid prescriptions. This may help us identify patients at risk after surgery and facilitate the setup of proactive measures like explicit taper to off plans to prevent unnecessary chronic opioid use.

Finally, unlike studies on medical patients and patients undergoing low-risk outpatient surgery, initial opioid prescription amount was not associated with higher risk of receiving additional post-operative opioid prescriptions. Brummett's study found patients to be at higher risk if receiving more than 300 MME or more but the effect size was small.[23] Many states have begun setting limits on the amount of opioids prescribed but there are concerns among many that arbitrary limits may negatively impact certain populations (e.g., major surgery, trauma and burn patients).[25] While over-prescribing is clearly a problem,[10,26] limits can be arbitrary and constrain providers unnecessarily. We support the ACS Statement on the Opioid Abuse Epidemic[25] and believe that a systematic approach, taking into account the opioids used during the hospitalization, the hospital course, and patient needs cared for by the surgeon acutely for surgical issues and by the primary care provider for other issues, can balance the needs of both society and the individual.

Limitations

A limitation of this study is its retrospective design at a single institution system. We were not able to capture opioid prescriptions outside this institution which could lead us to underestimate the number of patients requiring additional opioid prescriptions. However, limiting our study to a single-institution allowed us to examine the effects of a highly-protocol driven Enhanced Recovery Pathway with proven high compliance[7] conducted with the close collaboration of pharmacists. We were also able to look at pre-operative opioid prescribing up to 1 year prior to surgery. Another limitation is that we focused on the number of prescriptions given rather than patient consumption of tablets. We chose to do this because provider practices generate a large portion of the supply available for potential abuse. The majority of opioid overdoses are a result of friends or family sharing medications and the over-refilling of prescriptions is likely a key contributor.[27] Finally, we could not capture all of the psychosocial issues and prescriber biases that may contribute to opioid prescribing and this represents a potentially useful area of future research.

Conclusion

Additional opioid prescriptions after surgery occurred in 40% of patients. Pre-operative prescriptions, increasing operative time and complications were associated with additional opioid prescriptions while opioid amount at discharge was not a risk factor.

Conflicts of interest

None of the authors have conflicts of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.amjsurg.2018.12.003.

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