Original Article

The association between operation time and post-operative pain in endoscopic sinonasal surgery. Short title: Operative time and post-op pain after ESS

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Abstract

Background: United States is now in the midst of opioid crisis. To reduced perioperative opioid usage, is mean to reduce post-operative pain. This study try to find the association between operative time and post-operative pain in patient who received endoscopic sinonasal surgery. We also aim to study other factors that may play a role in post-operative pain.

Method: We performed a retrospective review of 624 patients, who have sinonasal disease and received endoscopic surgery from the same surgeon, in a tertiary care rhinology clinic from 2015 – 2018. Demographic data, diagnosis, duration of disease, Lund-Mackay CT score, operation, operation time, having bone drill, blood lost, time in PACU, and length of hospital stay were reviewed. For pain measurement we use patient self-reported visual analog scale from one to ten. Post-operative pain scale, intra-operative and post-operative analgesic usage were reviewed.

Result: One minute increasing in operation time will increase post-operative pain scale by 0.002 point ($P = 0.037$). When matched by same operation type, operation time still shows positive correlate with post-operative pain scale but lost its significant. Factors which positively associated with higher post-operative pain including: African American race; female; younger age (≤45 year old); and high BMI (all are $P < 0.05$). Increasing in duration of disease by ten months will decrease post-operative pain scale by 0.05 point ($P = 0.011$).

Conclusion: Operative time is associated with post-operative pain in endoscopic sinonasal surgery. The shorter the operation time, the less post-operative pain. Multiple factors both biological and psychological play a role in characterized individual pain experiences.

Keywords: Endoscopic sinus surgery, Pain, Post-operative pain, Operation time, Association, And opioid usage.

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Introduction

United States is now in the midst of facing opioid crisis from opioid epidemic. With more than 33,000 deaths per year, this has become nationwide public-health emergency.[1, 2] For many patients with an opioid use disorder, perioperative period is the first source of exposure, which may lead to persistence opioid usage.[3] By reducing post-operative pain, we may be able to reduce perioperative opioid usage. Many literatures try to identify factors that may contribute to post-operative pain such as demographic data, underlying disease, psychologic status, operation type, and operative technique.[4-10] Length of surgery is one of the possible factor that may affect post-operative pain, as longer operation time means more inflammation at surgical site.[11]

Surgeons from different fields, mainly in orthopedic and general surgery, tried to study the association between operation time and post-operative pain.[12-14] Their finding is noteworthy. In this study, we tried to assess the association between endoscopic sinonasal surgery's operation time and post-operative pain. In this way, we hope to provide the insight on how surgeon can contribute to alleviate opioid usage

Methods

We performed a retrospective study which reviewed medical records of sinonasal disease patients at sinonasal clinic of Stanford University Medical Center from 2015 to 2018. The Stanford Translational Research Integrated Database Environment (STRIDE) system was used for patient identification and data extraction. This project was approved by the Institutional Review board of Stanford University.

In the study group, inclusion criterias were age ≥ 18 years old, patients who were diagnosed with sinonasal disease, and received endoscopic sinus surgery from the same surgeon. Patients whose data went missing, didn't get admitted to post-anesthetic care unit (PACU), or received any open procedures in the same operation were excluded from this review.

Six hundred and forty eight patients were identified meeting the inclusion criteria. Twenty two patients were excluded due to missing data or received any open procedure in the same operation. Two patients didn't get admitted to post-anesthetic care unit (PACU), were also excluded. We then reviewed the medical records of the remaining 624 patients. Demographic data such as age, race, gender, and BMI were reviewed. Diagnosis, duration of disease, pre-operative Lund-Mackay CT score, type of operation, operation time, having bone drill, blood lost, time spend in PACU, and length of hospital stay were also reviewed. For pain measurement we use patient self-reported visual analog scale from one to ten. Post-operative pain scale was recorded every 30 minutes during the time patient spend in PACU. We use the maximum scale for the study. Intra-operative and post-operative analgesic usage were reviewed. Post-operative analgesic was used as needed according to patient's pain severity.

Statistical analysis

The statistical analysis was performed using SAS statistical software version 9.4 (SAS Institute, Inc, Cary, NC). Bivariable and multivariable model using robust regression were performed to evaluate the effect of variables on post-operative pain scale.

Results

Demographic Data

The demographic characteristics of patients are summarized in Table 1. The diagnosis consist of 326 (52.24%) chronic rhinosinusitis, 132 (21.15%) sinonasal tumor, 62 (9.94%) hereditary hemorrhagic telangiectasia, 10 (1.6%) fungal ball, 7 (1.12%) allergic fungal rhinosinusitis, 25 (4.01%) nasal obstruction, 4 (0.64%) invasive fungal sinusitis, 19 (3.04%) recurrent sinusitis, and 55 (8.81%) other diagnosis (mucocele, septal perforation, silent sinus syndrome, etc).

The operation consist of 2 (4.43%) unilateral endoscopic sinus surgery, 112 (17.95%) bilateral endoscopic sinus surgery, 13 (12.08%) unilateral endoscopic sinus surgery with septoplasty, 163 (26.12%) bilateral endoscopic sinus surgery with septoplasty, 57 (9.13%) limited endoscopic sinus surgery (< 2 out of 4 sinuses opened on each side), 116 (18.59%) nasal tumor surgery, 66 (10.58%) cauterization, 29 (4.65%) septoplasty, and 45 (7.21%) other surgery (marsupiallization, repair septal perforation, etc). Thirty seven (5.93%) of patients had bone drill during operation.

Intra-operative analgesic used during operation consist of 621 (99.52%) opioid injection, 2 (0.32%) fentanyl patch, 275 (44.55%) acetaminophen, 1 (0.16%) NSAID, and 1 (0.16%) no intra-operative analgesic use. Post-operative analgesic used as needed for severe pain consist of 441 (65.87%) opioid injection, 3 (0.48%) sedative agent, 115 (18.43%) acetaminophen, 320 (51.28%) oral opioid, 9 (1.44%) gabapentin, and 136 (21.79%) no post-operative analgesic use.

Association between operation time and post-operative pain.

The median operation time of overall cohort was 137.5 mins. The median post-operative pain scale was 5 point. Using bivariable robust regression model analysis, each one minute increasing in operation time will result in increasing post-operative pain scale by 0.007 point (P<0.05) (Table 2). In multivariable model, after control for patient's demographic data, duration of disease, and BMI, the result shows that one minute increasing in operative time will increase post-operative pain scale by 0.002 point (P=0.037) (Table 3). When matched by same operation type, multivariable model still shows positive correlate between operation time and post-operative pain scale but lost its significant. Only in cauterization procedure, which operation time still remain significant association with post-operative pain. (Table 4) This was due to small number of samples when divide into small groups.

We further perform analysis for chronic rhinosinusitis patients, using multivariable model control for patient's demographic data, duration of disease, and matched by pre-operative Lund-Mackay CT score. The result shows that operation time and post-operative pain scale are positively correlate but not significant (P = 0.241) (Table 5).

We also assessed whether other clinical variables demonstrated any association with post-operative pain after surgery. Bivariable analysis showed that the following variables were positively associated with higher post-operative pain: African American race; female; younger age (≤45 year old); and high BMI (all are P<0.05). On the other hand, longer disease duration by 10 months were negatively associated with post-operative pain (P<0.05) (Table 2). Further analysis using multivariable model showed that only young age, male, and BMI still remain significant association with post-operative pain (all are P<0.05) (Table 3).

Intra-operative bone drilling and intra-operative analgesic use did not demonstrate any significant association with post-operative pain (Table 2).

Post-operative analgesic usage correlate well with post-operative pain scale (Table 2). With lower pain scale (scale of 0-3), no medication was given. For higher pain scale: acetaminophen, opioid oral form, and opioid injection form, are given respectively.

Discussion

Opioid crisis is still a problem which need to be addressed in United States. Six percent of new persistent opioid-use patients had exposed to opioid first time during perioperative period.[15] By reducing post-operative pain, the demand for opioid usage will be reduced. Our study found that operation time is associated with post-operative pain. Each minute increasing in operation time, will result in increasing

post-operative pain scale. When matching by same operation type, operation time still positively associate with post-operative pain, but lost it significant. Only cauterization procedure still show significant association. Further analysis in only chronic rhinosinusitis patients also show positive correlation between operation time and post-operative pain scale, but not significant. This is due to reduction in sample size when divided them into several sub groups, causing the power to reduce. In the past, Kornilov et al[12] studied factors that may related to post-operative pain after total knee arthroplasty. They also found that total surgical time more than or equal to 90 mins increase post-operative pain.

The association between operation time and post-operative pain may be explained by the increasing in pro-inflammatory cytokine. Schwarz et al[11] reported association between operation time and local inflammation. They compare pro-inflammatory cytokine in portal and hepatic vein after hepatectomy using two different techniques. They found that using stapler technique, which significantly lower operation time, result in significantly lower pro-inflammatory cytokine (IL-6) and C-reactive protein.

Our study found other variables which also influence the post-operative pain. The younger age (≤ 45 year old), African American race, BMI, and female sex were all associate with increasing post-operative pain. Some studies in the past also found similar result. Kornilov et al[12] found that women reported more pain than men, and pre-operative anxiety significantly affect post-operative pain. Solheim et al[5] studied the effect of sex in immediate post-operative pain after knee arthroscopic surgery. They reported women has 4.9 times more likely to reported moderate to severe pain compare to men despite lower pro-inflammatory cytokine in synovial fluid. Logan et al[16] reported higher post-operative pain in adolescent girl compare to boy after surgery. Gagliese et al[17] reported older men has lower acute post-operative pain intensity compare to younger men. Perry et al[8] performed integrated literature reviewed and found that African Americans has significant higher post-operative pain intensity compare to Non-Hispanic whites. Cruz-Almeida et al[9] studied the effect of race on pain severity form osteoarthritis. They reported greater pain severity among African Americans than Non-Hispanic whites. Ostrom et al[18] also reported similar result in his orofacial pain cohort study. Guillemot-Legris et al[7] tried to study the effect of obesity on post-operative pain in mice. They found that obesity increase post-operative pain chronicization through several mechanism including increase inflammatory marker in both central and peripheral nervous system. To eliminate the potential confounding influence of these variables on the association between operation time and post-operative pain, we performed multivariable analysis, which controlled these variables. The result still showed a significant association between operation time and post-operative pain.

The experience of pain in each individual is different. Multiple variables, both biological and psychological factors, play a part in personalized pain experience. Moreover, these biopsychosocial factors, including demographic variables, genetic factors, inflammatory response, psychological stress, and pain catastrophizing, are also influence each other.[19] Our study showed that operation time is associated with post-operative pain. Although experience of post-operative pain depend on multiple factors, the result of this study should give surgeon some insight of their contribution in post-operative pain control. Contribution from multidisciplinary professions with well patient's education will reduce the need for opioid usage, contribute to alleviate

opioid crisis. This study was limited by retrospective methodology, which introduces inherent biases and limitations such as inadequacies in the medical record. Another limitation is the pain scale data can only be extracted from PACU database. Additional post-operative pain record at ward may reveal more accurate association. Further study should also include factors which might play a role in post-operative pain such as the effect of pre-operative analgesic.

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Table 1 Demographic data

Parameter	25 percentile	Median	75 percentile
Age	44	56	66
BMI	23.3	26.8	31.5
Duration of disease (Mo)	9	24	61
Post-operative pain score	2	5	7
Blood lost (Ml)	18	50	50
Operation time (Min)	74	137.5	192
Time in recovery room (Min)	111	143	185
Length of hospital stay (day)	1	1	1
Sex			
- Male		288 (46.15%)	
- Female		336 (53.85%)	
Race			
- Caucasian		411 (65.87%)	
- African American		25 (4.01%)	
- Asian		80 (12.82%)	
- Unknown or other		108 (17.31%)	

Data expressed as median or as number (%).

Table 2 Association between peri-operative variables and post-operative pain scale

Independent variables	Estimate	Lower	Upper	*P*
Operation time (Min)	0.007	0.004	0.010	0.000
African American	1.27	0.00	2.55	0.050
Asian	-0.69	-1.45	0.06	0.073
Other race	0.88	0.21	1.55	0.010
Female	1.09	0.58	1.60	0.000
Age	0.15	0.07	0.23	0.000
Duration (Mo)	-0.05	-0.09	-0.01	0.011
Intra-operative Bone drilling	0.12	-0.94	1.18	0.824
BMI	0.073	0.034	0.111	0.0003
Blood loss (Ml)	0.0003	-0.002	0.003	0.792
Intra-operative Opioid injection	-2.37	-5.97	1.24	0.198
Intra-operative Fentanyl patch	-0.01	-4.44	4.41	0.995
Intra-operative Acetaminophen	0.15	-0.36	0.65	0.570
Intra-operative NSAID	-2.52	-8.77	3.73	0.429
Intra-operative Oral opioid	-2.02	-6.44	2.40	0.370
Intra-operative No medication	-2.52	-8.77	3.73	0.429
Post-operative Opioid injection	5.03	4.7	5.36	0.000
Post-operative Oral opioid	2.36	1.90	2.81	0.000
Post-operative Acetaminophen	1.19	0.55	1.83	0.000
Post-operative No medication	-4.99	-5.41	-4.57	0.000

Analysis using bivariable robust regression model.

Values are significant at $P \leq 0.05$

BMI: body mass index

NSAID: non-steroidal anti-inflammatory drug

Table 3 Association between peri-operative variables and post-operative pain scale
Controlling for patient's demographics data, duration of disease, BMI, and perioperative analgesic use

Independent variables	estimate	lower	upper	*P*
Operation time (Min)	0.002	0.000	0.004	0.037
African American	0.012	-0.805	0.830	0.976
Asian	-0.090	-0.560	0.380	0.707
Other race	-0.086	-0.515	0.343	0.695
Female	0.498	0.187	0.809	0.002
Age	0.053	0.002	0.104	0.043
Duration (increase by 10 months)	-0.013	-0.037	0.011	0.290
BMI	0.030	0.004	0.055	0.022

Analysis using multivariable robust regression model, controlling for demographics, duration, BMI, when not use as independent variable.

Values are significant at $P \leq 0.05$

BMI: body mass index

Table 4 Association between operation time and post-operative pain score matched by operation type

Operation	Independent variables	Estimate	Lower	Upper	*P*
Unilateral ESS	Operation time	0.001	-0.024	0.022	0.957
	White	1.472	-0.732	3.676	0.191
	Male	1.735	-0.175	3.646	0.075
	Age	-0.036	-0.086	0.014	0.161
	Duration (increase by 10 months)	0.091	-0.182	0.364	0.514
Bilateral ESS	Operation time	0.001	-0.011	0.009	0.842
	African American	-1.345	-5.244	2.554	0.499
	Asian	-2.238	-3.665	-0.812	0.002
	Other race	1.034	-0.492	2.560	0.184
	Male	-1.491	-2.561	-0.421	0.006
	Age	-0.020	-0.057	0.016	0.270
	Duration (increase by 10 months)	-0.046	-0.111	0.019	0.164
Unilateral ESS	Operation time	0.003	-0.066	0.072	0.934
with septoplasty	White	0.071	-6.863	7.004	0.984
	Male	-1.125	-7.126	4.875	0.713
	Age	-0.026	-0.344	0.291	0.871
	Duration (increase by 10 months)	0.747	-0.881	2.375	0.368
Bilateral ESS	Operation time	0.006	-0.003	0.016	0.186
with septoplasty	African American	-2.290	-4.924	0.345	0.088
	Asian	0.163	-1.944	2.269	0.880
	Other race	0.033	-1.177	1.243	0.958
	Male	-0.910	-1.827	0.008	0.052
	Age	0.258	0.115	0.402	0.000
	Age 2	-0.003	-0.004	-0.001	0.000
	Duration (increase by 10 months)	-0.028	-0.099	0.043	0.438

Table 4 Association between operation time and post-operative pain score matched by operation type. (Ext.)

Operation	Independent variables	Estimate	Lower	Upper	*P*
Limited ESS	Operation time	0.010	-0.007	0.028	0.246
	African American	1.346	-5.407	8.099	0.696
	Asian	0.543	-1.774	2.860	0.646
	Other race	0.420	-2.224	3.064	0.755
	Male	-1.236	-3.143	0.672	0.204
	Age	-0.046	-0.399	0.307	0.800
	Age 2	0.001	-0.003	0.004	0.638
	Duration (increase by 10 months)	0.013	-0.188	0.214	0.901
Sinonasal tumor surgery	Operation time	0.003	-0.004	0.009	0.376
	African American	-0.245	-2.997	2.506	0.861
	Asian	-1.115	-2.751	0.521	0.182
	Other race	-0.447	-2.125	1.231	0.601
	Male	-0.325	-1.583	0.932	0.612
	Age	-0.057	-0.095	-0.018	0.004
	Duration (increase by 10 months)	0.009	-0.136	0.154	0.903
Cauterization	Operation time	0.075	0.036	0.114	0.000
	African American	5.327	2.965	7.689	0.000
	Asian	-0.984	-3.535	1.568	0.450
	Other race	-7.307	-12.397	-2.217	0.005
	Male	-1.668	-2.984	-0.351	0.013
	Age	0.274	0.093	0.456	0.003
	Age 2	-0.003	-0.005	-0.002	0.000
	Duration (increase by 10 months)	-0.073	-0.173	0.027	0.153
Septoplasty	Operation time	0.007	-0.021	0.036	0.618
	White	0.929	-2.207	4.065	0.561
	Male	-1.577	-4.489	1.336	0.289
	Age	-0.024	-0.111	0.062	0.582
	Duration (increase by 10 months)	-0.058	-0.247	0.130	0.543
Other operation	Operation time	0.012	-0.004	0.028	0.138
	African American	-0.674	-7.550	6.203	0.848
	Asian	-1.101	-3.886	1.685	0.439
	Other race	-0.431	-3.282	2.421	0.767
	Male	-1.158	-3.869	1.554	0.403
	Age	-0.003	-0.092	0.085	0.942
	Duration (increase by 10 months)	-0.016	-0.205	0.174	0.872

Analysis using multivariable robust regression model, controlling for demographics, duration, BMI, when not use as independent variable.

Values are significant at $P \leq 0.05$

BMI: body mass index

Table 5 Association between operation time and post-operative pain score in CRS patients. Controlling for patient's demographic data, duration of disease, and matched pre-operative Lund-Mackay CT score

Variable	Estimate	Lower	Upper	*P*
Operation time	0.004	-0.002	0.010	0.241
African American	-1.030	-3.327	1.266	0.379
Asian	-0.905	-1.982	0.173	0.100
Other race	0.419	-0.478	1.316	0.360
Male	-0.710	-1.371	-0.049	0.035
Age	0.216	0.110	0.322	0.000
Duration (increase by 10 months)	-0.046	-0.092	0.000	0.051
Pre-op LMS	-0.055	-0.114	0.005	0.074

Analysis using multivariable robust regression model, controlling for demographics, duration, BMI, and matched pre-operative Lund-Mackay CT score.

Values are significant at $P \leq 0.05$

BMI: body mass index

Pre-op LMS: pre-operative Lund-Mackay CT score

บทคัดย่อ

การศึกษาความสัมพันธ์ระหว่างระยะเวลาที่ใช้ในการผ่าตัดกับความเจ็บปวดหลังผ่าตัดโพรงจมูกและโพรงไซนัสด้วยการส่องกล้อง

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ที่มาและความสำคัญ: ประเทศอเมริกากำลังเผชิญปัญหาการใช้ยา opioid มากเกินความจำเป็น เพื่อลดการใช้ยาจำเป็นจะต้องลดความเจ็บปวดหลังผ่าตัดให้ได้ การศึกษานี้ทำขึ้นเพื่อหาความสัมพันธ์ระหว่างระยะเวลาที่ใช้ในการผ่าตัดกับความเจ็บปวดหลังผ่าตัดในผู้ป่วยที่ได้รับการผ่าตัดโพรงไซนัส และเพื่อหาปัจจัยต่างๆ ที่อาจส่งผลต่อความเจ็บปวดหลังผ่าตัด

ระเบียบวิธีวิจัย: การศึกษานี้เป็นการศึกษาย้อนหลังโดยการศึกษาประวัติผู้ป่วย 624 คน ซึ่งมีโรคทางโพรงไซนัสและเข้ารับการผ่าตัดโพรงไซนัสโดยการส่องกล้องที่โรงพยาบาลระดับตติยภูมิระหว่างปี 2015-2018 คณะผู้วิจัยได้วิเคราะห์ข้อมูลทั่วไป ข้อมูลเกี่ยวกับโรค ข้อมูลการผ่าตัดและการใช้ยาแก้ปวด สำหรับความเจ็บปวดหลังผ่าตัดจะถูกวัดในรูปแบบ visual analog scale จากคะแนน 1-10

ผลการศึกษา: ทุกๆ หนึ่งนาทีที่ใช้ในการผ่าตัดจะเพิ่มคะแนนความเจ็บปวดหลังผ่าตัด 0.002 คะแนน ($P = 0.037$) ชนชาติ African American เพศหญิง อายุน้อย และค่าดัชนีมวลกายที่สูงมีผลให้คะแนนความเจ็บปวดหลังผ่าตัดสูง ($P < 0.05$ ทั้งหมด) การเป็นโรคอยู่นานมีผลให้คะแนนความเจ็บปวดหลังผ่าตัดลดลง ($P < 0.011$)

สรุป: ระยะเวลาที่ใช้ในการผ่าตัดโพรงไซนัสที่น้อยลงส่งผลให้ความเจ็บปวดหลังผ่าตัดลดลง มีปัจจัยทั้งทางกายภาพและด้านจิตใจซึ่งส่งผลต่อการรับรู้ความเจ็บปวดของบุคคลแต่ละคนให้แตกต่างกัน

คำสำคัญ: การผ่าตัดโพรงไซนัสด้วยการส่องกล้อง, ความเจ็บปวดหลังผ่าตัด, ระยะเวลาผ่าตัด, ความสัมพันธ์, การใช้ยาแก้ปวดกลุ่ม opipoid