Effect of Smoking on Surgical Outcomes

Csaba Gajdos, MD
University of Colorado
Department of Surgery

Disclosure

- Nothing to disclose

Outline

- Background
- Second cancers and recurrence
- Wound healing
- Postoperative effect
- Conclusions

American Cancer Society Perspectives on Environmental Factors and Cancer

- "Within the realm of primary prevention, the ACS places the greatest priority on tobacco control, both because of the large cancer burden associated with this exposure and the availability of effective policy and medical interventions that are documented to reduce tobacco use and the burden of tobacco-related cancer"

Fontham ETH, CA Cancer J Clin 2009

Tobacco-related cancers

- Lung: leading cause of cancer death in the US: 160,340 in 2012
- Oral cavity
- Nasal cavity/sinuses
- Throat
- Esophagus
- Stomach
- Pancreas
- Kidney
- Bladder
- Uterus
- Cervix
- Colon/rectum
- Mucinous ovarian
- AML

Introduction

- Habitual tobacco use is the leading preventable cause of death in the US and is responsible for 1 of every 5 deaths
- A plateau was noted in the steady decline of percentage of smokers in the last decade
- In 2000, 25.7% of males and 21% of females were smokers
- In 2009 47 million people smoke almost daily in the US

Introduction

- In the US, approximately half of adult men reported smoking cigarettes in 1965 and many of these individuals did so for over 20 years
- Cigarette smoking accounts for approximately 30% of all cancer deaths and 80% of all lung cancer death in the general population
- Continued smoking after malignancy diagnosis may lead to a higher recurrence rate or second primary tumor compared to non-smokers

Introduction

- “Even our most conservative estimate indicates that reductions in lung cancer, resulting from reductions in tobacco smoking over the last half century, account for about 40% of the decrease in overall male cancer death rates and have prevented at least 146000 lung cancer deaths in men during the period 1991 to 2003.”

Thun et al. 2009, Tobacco Control

Introduction

(Dr David Raben's favorite study: showed negative effect of postoperative radiation on pancreas cancer survival)

"Log-rank analysis of the characteristics of patients and tumors revealed no significant differences in survival with respect to sex; an age of 60 years or more, as compared with less than 60 years; and the presence of preoperative diabetes, local invasion at operation, and postoperative complications, but borderline effects were found for current smoking (P=0.007), positive resection margins (P=0.10), and the presence of involved adjacent structures on histologic analysis (P=0.010). Increasingly differentiated tumors (P<0.001), the presence of lymph node involvement (P<0.001), and maximum tumor size (P=0.003) had significant effects on overall survival"

ESPAC 1; NEJM, 2004

Outline

- Background
- Second cancers and recurrence
- Wound healing
- Postoperative effect
- Conclusions

Second cancers and recurrence

- Current smokers have a 4 fold increased risk of a second aerodigestive tract cancer relative to non-smokers, but significant risk reduction is associated with smoking cessation
- General incidence of second malignancies 5-19% in head and neck cancer
- 40% of patients who continue to smoke develop recurrence or second malignancy, but rate drops to 6% for patients who stopped smoking

Second cancers and recurrence

- Chemoprevention studies showed a higher rate of developing second primary tumors for smokers (5.7%) compared with never smokers (3.5%) (lung, esophagus, bladder)

Smoking mechanism of action: cancer”

- P53 mutations are frequent in tobacco related cancer
- P 53 mutations were found in lung cancer, head and neck cancer, bladder cancer
- Mutation load is higher in cancers from smokers than from non-smokers

"Smoking mechanism of action: cancer"

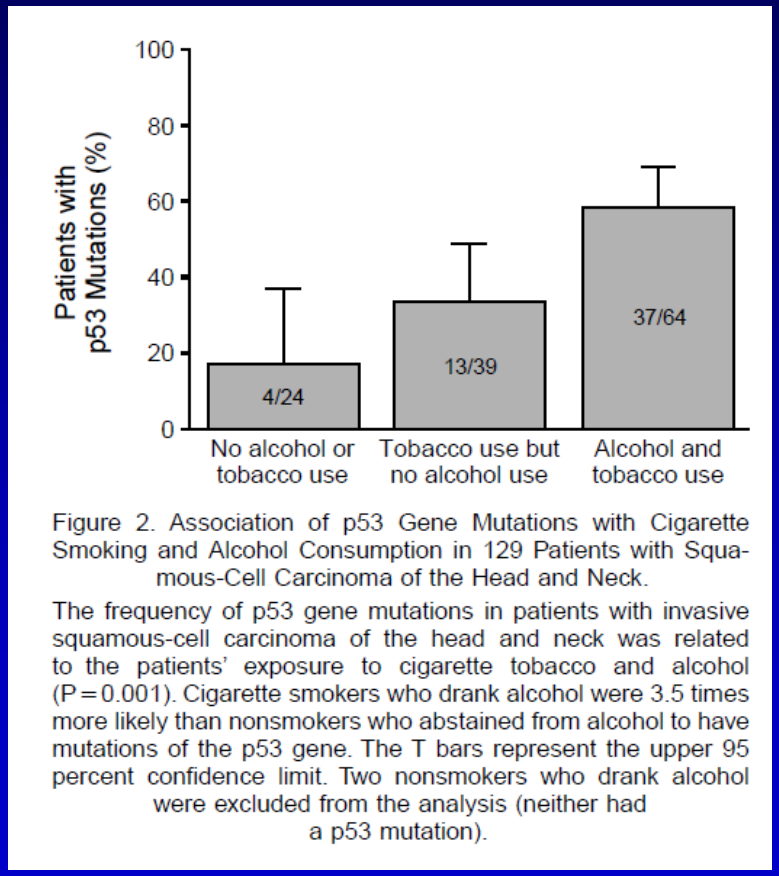
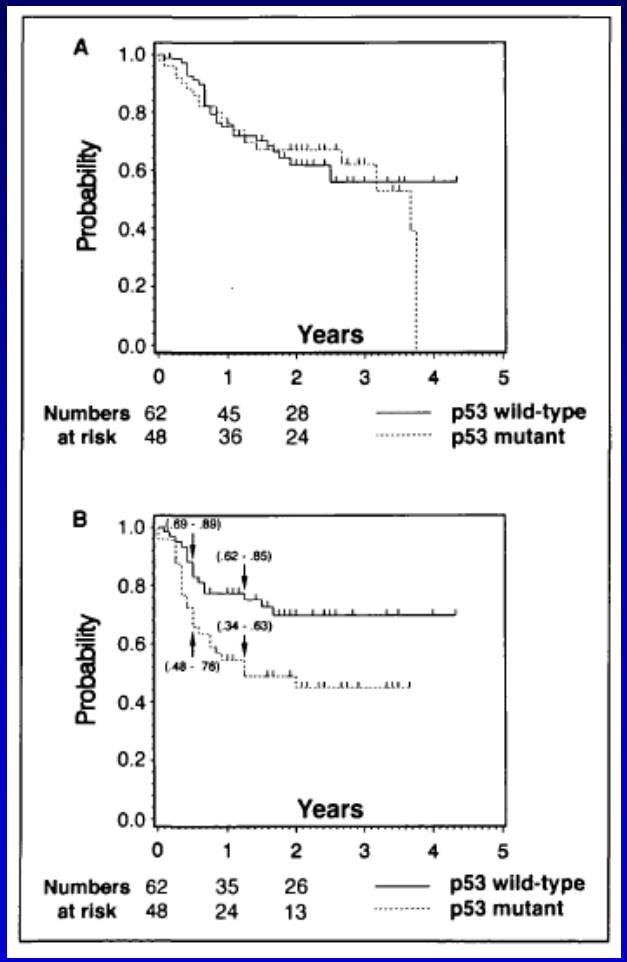


Figure 2. Association of p53 Gene Mutations with Cigarette Smoking and Alcohol Consumption in 129 Patients with Squamous-Cell Carcinoma of the Head and Neck.

The frequency of p53 gene mutations in patients with invasive squamous-cell carcinoma of the head and neck was related to the patients' exposure to cigarette tobacco and alcohol ($P = 0.001$). Cigarette smokers who drank alcohol were 3.5 times more likely than nonsmokers who abstained from alcohol to have mutations of the p53 gene. The T bars represent the upper 95 percent confidence limit. Two nonsmokers who drank alcohol were excluded from the analysis (neither had a p53 mutation).



Outline

- Background
- Second cancers and recurrence
- Wound healing
- Postoperative effect
- Conclusions

“Smoking mechanism of action: complications”

- Hypoxia-reduced collagen production
- Modified function of bactericidal activity of neutrophils
- Diseased microcirculation leading to poor anastomotic healing
- Nitric oxide production affecting platelet aggregation
- Raised serotonin concentrations affecting smooth muscle in mesenteric vessel
- Alveolar macrophage antimicrobial function and increased sputum production

“Smoking mechanism of action: complications”

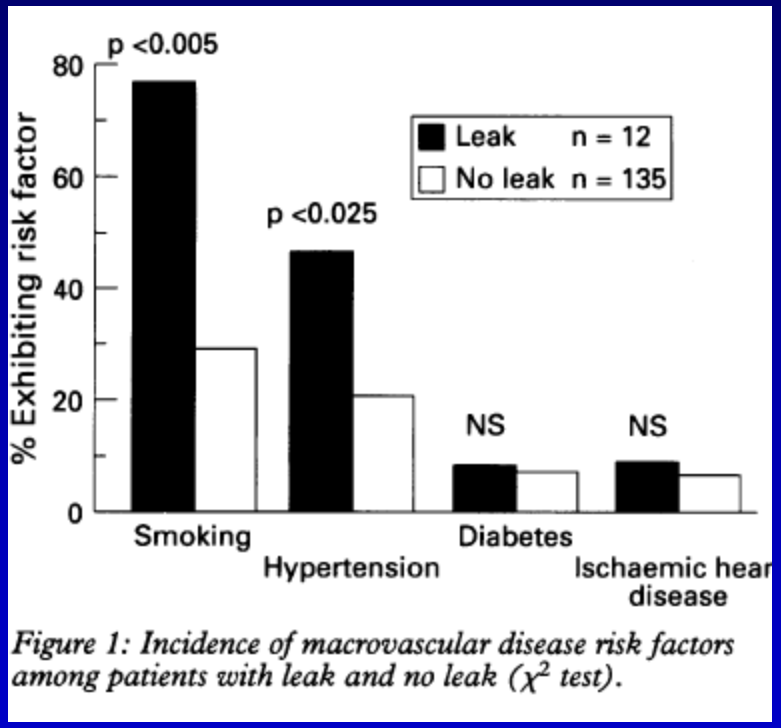


Figure 1: Incidence of macrovascular disease risk factors among patients with leak and no leak (χ^2 test).

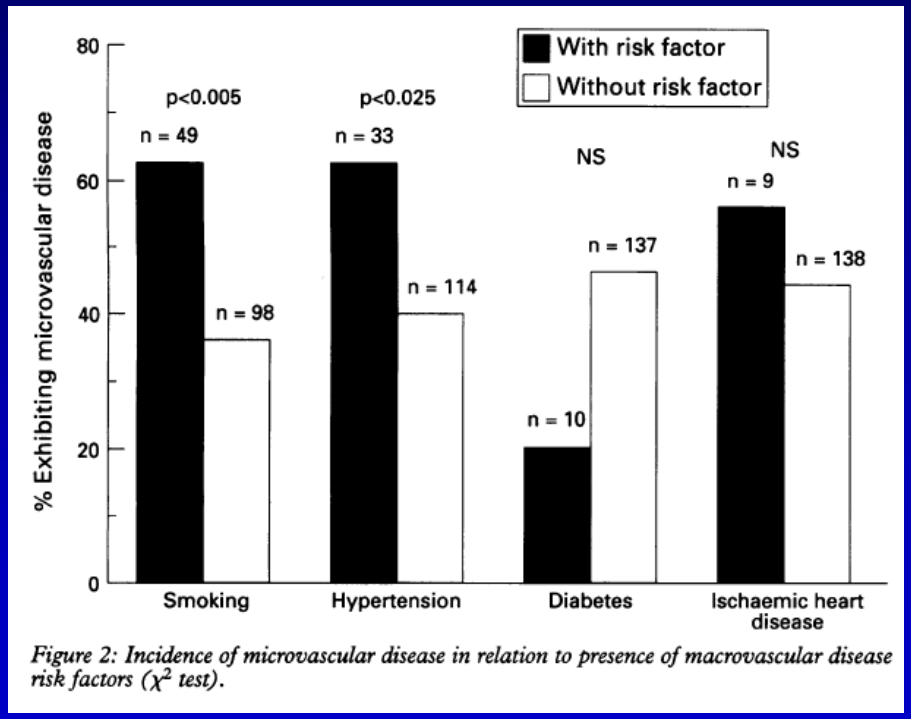


Figure 2: Incidence of microvascular disease in relation to presence of macrovascular disease risk factors (χ^2 test).

Abstinence From Smoking Reduces Incisional Wound Infection:

A Randomized Controlled Trial

Lars Tue Sorensen, MD,† Tonny Karlsmark, MD, DMSci,* and Finn Gottrup, MD, DMSci**

- 78 healthy subjects (48 smokers/30 never smokers) were followed for 15 weeks
- Smokers smoked for a week
- At 1 week smokers were randomized to continuous smoking and abstinence
- Wounds were made via punch bx at 1/4/8/12 weeks lateral to the sacrum

Results

TABLE 1. Baseline Characteristics of Subjects

	Smokers	Never-smokers
Women/men	24/24	15/15
Age (y), median (range)	33 (20–40)	26‡ (20–40)
Cigarettes per day, median (range)	20 (10–50)	0‡ (0–0)
Pack-years,* median (range)	16 (3–50)	0‡ (0–0)
Fagerstrom score, median (range)	6 (0–10)	0‡ (0–0)
Alcohol per week,† median (range)	4 (0–30)	4 (0–15)
Body mass index, mean ± SD	23.4 ± 4.1	23.1 ± 3.6
Carboxyhemoglobin, fraction, median (range)	0.04 (0.02–0.08)	0.01‡ (0.01–0.02)
Hemoglobin mmol/L, mean ± SD	8.8 ± 0.6	8.5 ± 0.7
Neutrophils billions/L, mean ± SD	4.5 ± 1.6	3.2‡ ± 1.3

*Cigarettes per day/20 × years of smoking.
†Sum of one bottled beer, one glass of wine, and one measure of spirits equivalent to 9–13 g of alcohol.
‡Different to smokers' value, $P < 0.05$.
SD, standard deviation.

Results

TABLE 2. Blood Values in Smokers After Randomization to Continuous Smoking or Abstinence

	Continous-smokers (n = 16)	Abstinent-smokers (n = 32)
4 weeks after randomization		
Carboxyhemoglobin fraction, median (range)	0.05 (0.03–0.06)	0.01* (0.01–0.03)
P-Cotinine ng/mL, median (range)	291 (100–548)	99* (0–262)
Hemoglobin mmol/L, mean ± SD	9.0 ± 0.6	8.7 ± 0.7
Neutrophils billions/L, mean ± SD	4.6 ± 1.3	3.8* ± 1.1
8 weeks after randomization		
Carboxyhemoglobin fraction, median (range)	0.05 (0.02–0.06)	0.01 (0.01–0.05)
P-Cotinine ng/mL, median (range)	307 (138–597)	161* (0–431)
Hemoglobin mmol/L, mean ± SD	9.0 ± 0.7	8.8 ± 0.8
Neutrophils billions/L, mean ± SD	4.7 ± 1.8	4.1 ± 1.4
12 weeks after randomization		
Carboxyhemoglobin fraction, median (range)	0.05 (0.02–0.08)	0.01* (0.01–0.05)
P-Cotinine ng/mL, median (range)	347 (108–578)	65* (0–480)
Hemoglobin mmol/L, mean ± SD	8.8 ± 0.64	8.7 ± 0.72
Neutrophils billions/L, mean ± SD	4.8 ± 1.67	3.9* ± 1.05

*Different to continuous smokers' value $P < 0.05$.
SD, standard deviation.

Results

- Total wound infection rate in smokers was 12% compared with 2% in non-smokers
- Wound infections were significantly fewer in the abstinent group (1 patient) compared with the continued smoking group (10 patients) after weeks of randomization
- These results did not significantly change at 8 and 12 weeks

Conclusion

- Healthy smokers have a higher incidence of wound infections than never-smokers and 4 weeks of abstinence form smoking reduces wound infections to a level similar to never-smokers

Outline

- Background
- Second cancers and recurrence
- Wound healing
- Postoperative effect
- Conclusions

Risk Factors for Tissue and Wound Complications in Gastrointestinal Surgery

Lars Tue Sørensen, MD, Ulla Hemmingsen, RN,* Finn Kallehave, MD,* Peer Wille-Jørgensen, MD, DmSci,* Johan Kjærgaard, MD, DmSci,* Lisbeth Nørgaard Møller, MS,† and Torben Jørgensen, MD, DmSci†*

- Retrospective review of 4855 cases undergoing open GI surgery between 1995-1998
- Complications resulted in prolonged hospitalization in 50% of the patients and a 3-fold higher risk of reoperations

Results

TABLE 3. Variables Associated With Tissue and Wound Complications Following Elective Operation Analyzed by Logistic Regression: The Final Model*

	Univariate		Multivariate	
	OR	95% CI	OR	95% CI
Smoking status				
Nonsmoker	1	—	1	—
Smoker	1.73	1.26–2.36	1.76	1.27–2.43
Comorbidity†				
No	1	—	1	—
Yes	1.41	1.00–1.99	1.47	1.45–2.07
Blood loss				
<100 mL	1	—	1	—
100–500 mL	3.35	2.24–5.05	1.70	1.00–2.91
>500 mL	8.75	5.87–13.02	3.82	2.19–6.68
Operation				
Hernia surgery	1	—	1	—
Biliary surgery	0.98	0.52–1.87	0.83	0.43–1.59
Gastroduodenal surgery	3.48	1.13–10.71	2.07	0.58–7.40
Small-bowel surgery	4.42	2.31–8.44	2.84	1.41–5.70
Colorectal surgery	7.08	4.70–10.68	3.21	1.79–5.74

*Cases included in the model: 3148; cases rejected due to missing data: 217.

†Diabetes, cardiovascular disease, or lung disease. Variables significantly associated with tissue and wound complications in the univariate analysis, but failed to be significant in the final multivariate model were family status, multiple operations, malignancy, reoperation, and surgeon's training.

ARTICLES

Effect of preoperative smoking intervention on postoperative complications: a randomised clinical trial

Ann M Møller, Nete Villebro, Tom Pedersen, Hanne Tønnesen

- Randomized trial enrolling 120 patients undergoing knee and hip replacement in Denmark
- Randomly assigned to control or smoking intervention group 6-8 weeks before surgery
- Smoking intervention group has counseling and nicotine replacement therapy resulting in smoking cessation or 50% reduction

ARTICLES

Effect of preoperative smoking intervention on postoperative complications: a randomised clinical trial

Ann M Møller, Nete Villebro, Tom Pedersen, Hanne Tønnesen

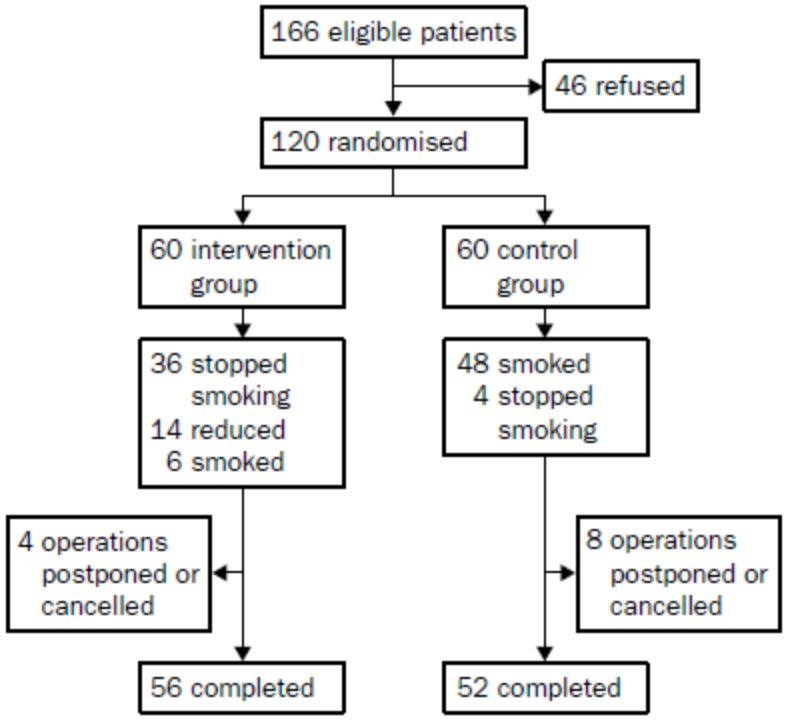


Figure 1: **Trial profile**

	Intervention group (n=56)	Control group (n=52)	p
Preoperative factors			
Age (years)	66 (41–83)	64 (30–85)	0·37
Women	32 (57%)	30 (58%)	0·85
Body-mass index (kg/m²)	27 (15–43)	26 (17–44)	0·64
ASA class			
I	23 (41%)	16 (31%)	0·86
II	31 (56%)	33 (63%)	
III	2 (3%)	3 (6%)	
History of disease			
Chronic heart disease	7 (12%)	8 (15%)	0·33
Chronic obstructive lung disease	7 (13%)	5 (10%)	0·52
Diabetes mellitus	1 (2%)	3 (5%)	0·41
Preoperative laboratory tests			
Haemoglobin (g/L)	139 (118–174)	135 (96–155)	0·22
Creatinine (μmol/L)	84 (61–121)	81 (57–170)	0·38
FEV_1 (L/s)	2·2 (0·8–4·5)	2·3 (1·2–4·6)	0·63
Smoking habits			
Cigarettes per day	15 (5–30)	15 (3–30)	0·71
Pack years*	35 (11–65)	37 (1–102)	0·61
Intraoperative factors			
General anaesthesia	28 (50%)	33 (63%)	0·22
Knee replacement	16 (29%)	17 (33%)	0·68
Hip replacement	40 (71%)	35 (67%)	0·68
Duration of surgery (min)	90 (35–160)	90 (45–190)	0·92

Data are median (range) or number (%). ASA=American Society of Anesthesiology Physical Status Score; FEV_1=forced expiratory volume in 1 s.
*Smoking years×daily consumption=20.

Table 1: **Patients' baseline characteristics**

ARTICLES

Effect of preoperative smoking intervention on postoperative complications: a randomised clinical trial

Ann M Møller, Nete Villebro, Tom Pedersen, Hanne Tønnesen

	Intervention group (n=56)	Control group (n=52)	p
Complications*			
Respiratory insufficiency†	1 (2%)	1 (2%)	0·97
Cardiovascular insufficiency‡	0	5 (10%)	0·08
Renal insufficiency§	0	1 (2%)	0·98
Delirium or confusion¶	1 (2%)	4 (8%)	0·15
Gastrointestinal bleeding¶	0	1 (2%)	0·98
Wound-related	3 (5%)	16 (31%)	0·001
Haematoma	1 (2%)	4 (8%)	
Infection (positive culture)	2 (4%)	12 (23%)	
Subfascial involvement	1 (2%)	4 (8%)	
Urinary tract infection‖	5 (9%)	6 (12%)	0·66
Any	10 (18%)	27 (52%)	0·0003
Death	0	0	..
Secondary surgery	2 (4%)	8 (15%)	0·07
Replacement	0	0	
Reposition	1 (2%)	0	
Wound-related	1 (2%)	7 (13%)	
Vascular	1 (2%)	1 (2%)	
Hospital stay			
Orthopaedic department (days, median [range])	11 (7–55)	13 (8–65)	0·41
Total days in orthopaedic department	750	767	
Total days in non-orthopaedic department	2	49	
In medical or surgical departments	0	17	
In intensive-care unit	2	32	

Data are number of patients (%) unless otherwise indicated. *Patients might have more than one complication; †requiring ventilatory support in intensive-care unit; ‡myocardial infarction or congestive heart failure; §creatinine >300 μmol/L or dialysis; ¶requiring treatment; ‖positive culture treated with antibiotics.

Table 2: **Outcomes in the two study groups**

ARTICLES

Effect of preoperative smoking intervention on postoperative complications: a randomised clinical trial

Ann M Møller, Nete Villebro, Tom Pedersen, Hanne Tønnesen

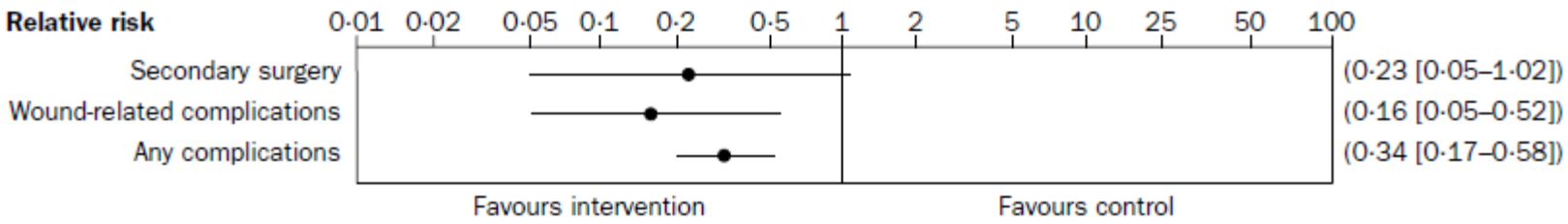
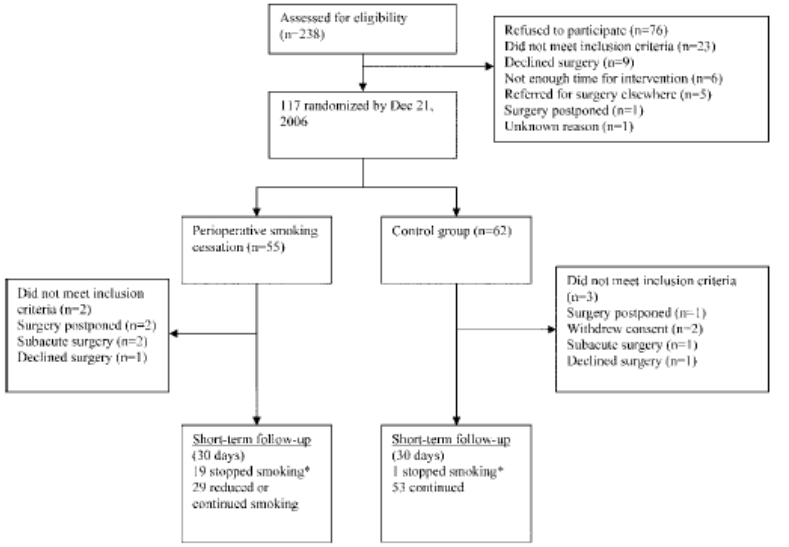


Figure 2: **Relative risk of postoperative events**
Bars=95% CI.

An effective smoking intervention programme applied 6–8 weeks before surgery more than halved the frequency of postoperative complications, with the greatest effect on wound-related and cardiovascular complications. Although the exact duration of smoking abstinence necessary cannot be concluded from these data, we recommend cessation of smoking for at least 6 weeks on the basis of our results.

Effects of a Perioperative Smoking Cessation Intervention on Postoperative Complications

A Randomized Trial



* Abstinence defined here by smoking zero cigarettes for a minimum period of three weeks prior to surgery until four weeks postoperatively with the additional criterion that the exhaled carbon monoxide level postoperatively did not exceed 10 ppm.

TABLE 5. Per Protocol Analysis. Postoperative Complications Within 30 Days in Relation to Perioperative Abstinence Period

	Stopped Smoking ≥3 Week Preoperatively* (n = 20)	Stopped Smoking 1 to 2 Week Preoperatively† (n = 9)	Continued Smoking (n = 73)	*P*
Any wound complication, No. (%)	2 (10)	0 (0)	18 (25)	0.10‡
Any complication, No. (%)	3 (15)	2 (22)	27 (37)	0.14‡

*Abstinence defined by smoking zero cigarettes for a minimum period of 3 week before surgery until 4 week postoperatively and postoperative carbon monoxide ≤10 ppm.

†Abstinence defined by smoking zero cigarettes for a period of 1 to 2 week before surgery until 4 week postoperatively and postoperative exhaled carbon monoxide level ≤10 ppm.

‡χ^2 (2-sided).

Outcomes in cancer surgery

- There is conflicting evidence regarding the attributable risk of smoking on post-operative complications
- Cancer patients have higher prevalence of smoking and may be at higher incidence of smoking related complications
- Postoperative complications have been shown to result in an omission or significant delay in the initiation of adjuvant chemotherapy in colon and rectal cancer

Outcomes in cancer surgery

- The negative effects of smoking may not be uniform across various disease sites
- There is evidence that smokers have an increased risk of postoperative complications and possibly death in general and thoracic surgery patients, this area has not been well-studied for major gastro-intestinal surgeries.

Predictors of major morbidity and mortality after esophagectomy for esophageal cancer: A Society of Thoracic Surgeons General Thoracic Surgery Database risk adjustment model

Cameron D. Wright, MD,[a] John C. Kucharczuk, MD,[b] Sean M. O'Brien, PhD,[c] Joshua D. Grab, MS,[c] and Mark S. Allen, MD[d]

- 2315 esophagectomies performed in 73 centers
- Major morbidity and mortality were evaluated
- 75% of patients were smokers

Results

TABLE 3. Predictors of major morbidity after esophagectomy for cancer

Variable	Odds ratio		*P* value
	Estimate	95% CI	
Age (y)			
65 vs 55	1.04	0.90–1.20	.593
75 vs 55	1.24	1.07–1.45	.005
Female	1.20	0.92–1.55	.177
Black race	1.76	0.93–3.34	.082
CHF	2.3	1.18–4.49	.015
CAD	1.31	1.05–1.65	.017
PVD	1.55	1.12–2.14	.009
Zubrod score			
1 vs 0	1.13	0.98–1.30	.100
2 vs 0	1.27	0.95–1.69	.100
3 vs 0	1.43	0.93–2.20	.100
4 vs 0	1.62	0.91–2.86	.100
ASA class			
2 vs 1	1.26	1.10–1.46	.001
3 vs 1	1.60	1.20–2.13	.001
4 vs 1	2.02	1.32–3.10	.001
5 vs 1	2.56	1.45–4.52	.001
Insulin diabetes	1.19	1.05–1.36	.009
Hypertension	1.16	1.01–1.32	.029
Steroids	1.81	1.07–3.06	.026
Renal dysfunction	0.95	0.55–1.64	.846
Induction therapy	0.93	0.77–1.11	.424
Cigarette usage	1.27	1.03–1.56	.022
BMI (per 5-unit increase)	1.02	1.00–1.03	.123
Time trend (per 5 y)	1.29	0.93–1.80	.133

ASA, American Society of Anesthesiology; *BMI*, body mass index; *CAD*, coronary artery disease; *CHF*, congestive heart failure; *CI*, confidence interval; *PVD*, peripheral vascular disease.

Predictors of Prolonged Length of Stay after Lobectomy for Lung Cancer: A Society of Thoracic Surgeons General Thoracic Surgery Database Risk-Adjustment Model

Cameron D. Wright, MD, Henning A. Gaissert, MD, Joshua D. Grab, MS, Sean M. O'Brien, PhD, Eric D. Peterson, MD, MPH, and Mark S. Allen, MD

- 4979 lobectomies performed at 56 sites were reviewed
- Predictors of prolonged length of stay were evaluated
- Over 80% of patients were smokers

Results

Table 3. Patient Characteristics in Those With and Without a Prolonged Length of Stay

	LOS < 14 Days		LOS > 14 Days		
Variable	No.	Age	No.	Age	*p* Value
Age, median years	4628	68	351	71	<0.0001
	No	%	No.	%	
Gender					
Female	2365	51	133	38	<0.0001
Male	2263	49	218	62	
Zubrod score					
1	2079	6	115	33	<0.0001
2	2024	45	172	49	
3	182	44	36	10	
4	50	1	7	2	
5	5	0.10	2	0.60	
Insulin-dependent diabetes					
Yes	123	21	19	33	0.038
No	454	79	38	67	
Renal dysfunction					
Dialysis	15	0.30	6	1.70	<0.0001
Creatinine >2 mg/dL	84	1.80	13	3.70	
None	4529	98	332	95	
Induction therapy					
Yes	495	11	55	16	0.037
No	4133	89	296	84	
Smoking					
Yes	3912	85	323	92	0.0007
No	716	15	28	8	
FEV_1, %predicted mean	4628	81	351	74	<0.0001
ASA score					
1	110	2	4	1	<0.0001
2	1154	25	45	13	
3	2570	56	220	63	
4	353	8	55	16	
Cardiovascular disease[a]					
Yes	1232	27	137	39	<0.0001
No	3396	73	214	61	

Impact of Smoking Cessation Before Resection of Lung Cancer: A Society of Thoracic Surgeons General Thoracic Surgery Database Study

David P. Mason, MD, Sreekumar Subramanian, MD, Edward R. Nowicki, MD, MS, Joshua D. Grab, MS, Sudish C. Murthy, MD, PhD, Thomas W. Rice, MD, and Eugene H. Blackstone, MD

- 7990 primary resections for lung cancer studied
- Risk of in-hospital death and respiratory complications were assesed according to timing of smoking cessation

Results

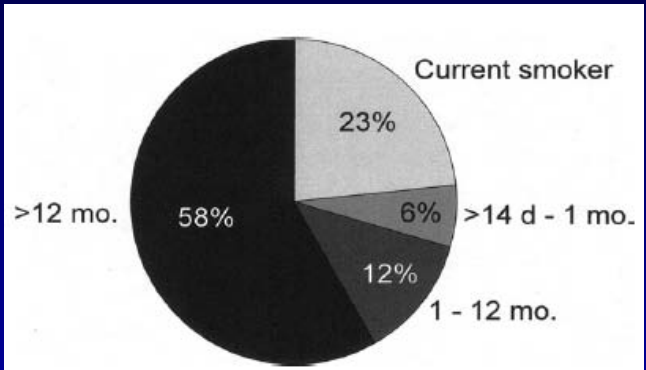


Fig 1. Interval of smoking cessation before resection for lung cancer among 6941 patients with a history of smoking.

Table 2. Outcome After Resection for Lung Cancer According to Smoking Status

Category	Overall No. (% of 7990)	Hospital Mortality No. (%)	Overall No. (% of 7965)[a]	Pulmonary Complications No. (%)
Current smoker	1595 (20)	24 (1.5)	1590 (20)	110 (6.9)
Pre-op smoking cessation interval				
>14 d–1 mo	404 (5.1)	7 (1.7)	402 (5.0)	25 (6.2)
1–12 mo	940 (12)	12 (1.3)	938 (12)	60 (6.4)
>12 mo	4026 (50)	62 (1.5)	4011 (50)	234 (5.8)
Never smoked[b]	1025 (13)	4 (0.39)	1024 (13)	27 (2.6)
Total	7990 (100)	109 (1.4)	7965 (100)	456 (5.7)

[a] Excludes 25 patients who died on the day of operation. [b] Includes patients who smoked fewer than 100 cigarettes in their lifetime.

Results

Table 3. Multivariable Logistic Model of Hospital Mortality After Resection for Lung Cancer

Variable	Coefficient ± SE	Est OR (95% CL)	*p* Value
Current smoker[a]	1.2 ± 0.58	3.5 (1.1, 11)	0.03
Pre-op smoking cessation interval			
>14 d–1 mo[a]	1.5 ± 0.70	4.6 (1.2, 18)	0.03
1–12 mo[a]	0.96 ± 0.71	2.6 (0.65, 11)	0.2
>12 mo[a]	0.91 ± 0.57	2.5 (0.82, 7.6)	0.1
Age	0.054 ± 0.015	1.1 (1.03, 1.09)	0.0002
Body mass index	−0.013 ± 0.027	0.99 (0.94, 1.0)	0.6
Pack-years	−0.0017 ± 0.0054	1.00 (0.99, 1.01)	0.8
FEV_1 (% of predicted)	−0.012 ± 0.0049	0.99 (0.98, 1.00)	0.01
Female	0.016 ± 0.20	1.02 (0.68, 1.5)	0.9
Zubrod score	−0.021 ± 0.19	0.98 (0.67, 1.43)	0.9
ASA risk class	0.34 ± 0.17	1.4 (1.01, 1.9)	0.04
Hypertension	0.16 ± 0.21	1.2 (0.78, 1.8)	0.4
Steroids	0.66 ± 0.42	1.9 (0.85, 4.4)	0.11
Heart failure	0.53 ± 0.34	1.7 (0.87, 3.3)	0.12
Coronary artery disease	0.35 ± 0.24	1.4 (0.88, 2.3)	0.15
Peripheral arterial disease	0.74 ± 0.22	2.1 (1.4, 3.2)	0.0006
Rx-treated diabetes	−1.3 ± 0.70	0.27 (0.06, 1.2)	0.08
Renal insufficiency	0.74 ± 0.31	2.1 (1.2, 3.8)	0.02
Pre-op chemo and/or radiotherapy	0.49 ± 0.28	1.6 (0.94, 2.8)	0.08
Cancer stage pT	0.099 ± 0.17	1.1 (0.79, 1.5)	0.6
Cancer stage pN	0.26 ± 0.14	1.3 (0.97, 1.7)	0.08
Lobectomy	0.37 ± 0.32	1.4 (0.77, 2.7)	0.2
Pneumonectomy	1.5 ± 0.40	4.3 (2.0, 9.5)	0.0002

[a] Versus never smoked.

ASA = American Society of Anesthesiologists; CLs = confidence limits; FEV_1 = forced expiratory volume in 1 second; OR = odds ratio; Rx = pharmacologically; SE = standard error.

ORIGINAL ARTICLE – HEALTHCARE POLICY AND OUTCOMES

Adverse Effects of Smoking on Postoperative Outcomes in Cancer Patients

- VASQIP database with operations between 2002-2008
- ICD-9 and CPT codes were used to select cancer cases, all emergent operations excluded (n=20413)
- Divided into GI (n=12432) thoracic (n=4490) and urologic (n=3491) malignancies
- Patients further divided into current, prior and never smokers
- Rates of smokers (current and prior) GI 51%; thoracic 84%; urologic 57%

Results

TABLE 1 Patient characteristics by smoking status in cancer patients, % (*n*) or mean (SD)

	Overall (n = 20,413)	Never smoked (n = 8,375)	Prior smoker (n = 5,096)	Current smoker (n = 6,942)	P value
Patient demographics					
Male gender	97.8 (19,961)	97.6 (8,172)	98.6 (5,023)	97.5 (6,766)	<.001
Race					<.001
White, Hispanic	4.1 (842)	5.9 (497)	3.1 (156)	2.7 (189)	
Black	15.1 (3,089)	15.3 (1,282)	11.8 (601)	17.4 (1,206)	
White, not of Hispanic origin	63.8 (13,032)	61.9 (5,181)	68.0 (3,465)	63.2 (4,386)	
Unknown/other	16.9 (3,450)	16.9 (1,415)	17.2 (874)	16.7 (1,161)	
Age, mean (SD)	66.6 (10.2)	68.8 (10.4)	69.3 (9.3)	62.1 (9.0)	<.001
Pack years of smoking, mean (SD)	37.9 (39.0)	0.0 (0.0)	49.2 (36.3)	59.1 (34.7)	<.001
Preoperative status					
Diabetes	23.2 (4,733)	26.9 (2,249)	26.2 (1,333)	16.6 (1,151)	<.001
ETOH >2 drink a day 2 weeks. before admission	11.0 (2,231)	6.0 (497)	8.4 (429)	18.9 (1,305)	<.001
Chemotherapy for malignancy in last 30 days	1.7 (343)	1.4 (120)	1.6 (79)	2.1 (144)	.006
Congestive heart failure in 30 days before surgery	1.6 (325)	1.7 (139)	2.0 (101)	1.2 (85)	.004
History of severe COPD	20.5 (4,189)	9.7 (815)	24.9 (1,270)	30.3 (2,104)	<.001
Open wound/wound infection	1.0 (211)	1.0 (83)	1.0 (52)	1.1 (76)	.814
>10% loss of body weight in last 6 months	10.4 (2,114)	8.6 (722)	9.9 (505)	12.8 (887)	<.001
Functional health status (1–3)					<.001
Independent	94.7 (19,324)	93.9 (7,863)	94.5 (4,816)	95.7 (6,645)	
Partially dependent	4.8 (972)	5.4 (450)	5.0 (256)	3.8 (266)	
Totally dependent	0.6 (117)	0.7 (62)	0.5 (24)	0.4 (31)	
Preoperative serum albumin, mean (SD)	3.8 (0.6)	3.8 (0.6)	3.8 (0.5)	3.8 (0.6)	.004

Results

Smoking and Cancer Surgery Outcomes

TABLE 2 Postoperative outcomes by smoking status in cancer patients

	Overall (n = 20,413)	Never smoked (n = 8,375)	Prior smoker (n = 5,096)	Current smoker (n = 6,942)	P value
Surgical site infection	8.9 (1,824)	8.9 (744)	9.8 (498)	8.4 (582)	.030
Venous thromboembolism	1.3 (263)	1.3 (110)	1.7 (89)	0.9 (64)	<.001
Stroke/cerebrovascular accident	0.5 (106)	0.4 (37)	0.8 (39)	0.4 (30)	.019
Myocardial infarction	0.9 (178)	0.8 (68)	1.2 (63)	0.7 (47)	.004
Renal failure	2.1 (436)	2.0 (170)	2.8 (144)	1.8 (122)	<.001
Urinary tract infection	3.9 (799)	4.1 (340)	4.7 (238)	3.2 (221)	<.001
Pneumonia	7.3 (1,497)	4.9 (409)	8.2 (417)	9.7 (671)	<.001
Failure to wean	5.1 (1,048)	3.4 (282)	5.7 (293)	6.8 (473)	<.001
Reintubation	5.8 (1,183)	3.8 (322)	6.4 (328)	7.7 (533)	<.001
30-day mortality	3.4 (698)	2.9 (242)	4.6 (236)	3.2 (220)	<.001
1-year mortality*	16.1 (3,292)	13.5 (1,127)	18.5 (941)	17.7 (1,224)	<.001
Pulmonary complication (CPO)	11.1 (2,272)	7.8 (651)	12.5 (638)	14.2 (983)	<.001
Vascular complication	1.4 (277)	1.2 (103)	2.0 (100)	1.1 (74)	<.001
Composite outcome	19.1 (3,901)	16.0 (1,343)	21.2 (1,078)	21.3 (1,480)	<.001
Return to OR	9.4 (1,929)	8.1 (680)	9.8 (498)	10.8 (751)	<.001
Length of postoperative surgical stay, mean (SD)	10.3 (10.7)	9.8 (10.5)	10.7 (11.0)	10.6 (10.8)	<.001
Excluding those with 30-day mortality	10.3 (10.8)	9.8 (10.5)	10.7 (11.1)	10.6 (10.9)	<0.001

Results are presented as column-% (n) unless specified otherwise. For patients with 30-day mortality, it is unknown whether death occurred prior to hospital discharge

Comparison of never smokers to current and prior smokers

TABLE 3 Comparison of current and prior smokers, using never smokers as a reference group

Cancer site/smoking status	Odds ratio (95% confidence interval)							
	Surgical site infection	Pneumonia	Failure to wean	Reintubation	Combined pulmonary outcome	Return to OR	30-day mortality	1-year mortality
GI, $n = 12{,}432$								
Never (49%)	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Prior (25%)	1.25 (1.09–1.44)	1.52 (1.26–1.84)	1.58 (1.28–1.97)	1.66 (1.35–2.04)	1.60 (1.38–1.87)	1.20 (1.03–1.39)	1.50 (1.19–1.89)	1.22 (1.08–1.38)
Current (26%)	1.20 (1.05–1.38)	1.98 (1.64–2.40)	2.21 (1.79–2.73)	2.15 (1.75–2.65)	1.96 (1.68–2.29)	1.31 (1.13–1.53)	1.41 (1.08–1.82)	1.62 (1.43–1.85)
Thoracic, $n = 4{,}490$								
Never (16%)	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Prior (29%)	0.69 (0.38–1.26)	1.05 (0.76–1.44)	1.15 (0.76–1.74)	1.11 (0.77–1.60)	1.08 (0.81–1.42)	0.97 (0.68–1.39)	1.43 (0.88–2.34)	1.19 (0.92–1.54)
Current (55%)	0.93 (0.54–1.60)	1.51 (1.12–2.03)	1.64 (1.11–2.40)	1.72 (1.22–2.42)	1.62 (1.25–2.11)	1.30 (0.94–1.81)	1.30 (0.79–2.13)	1.50 (1.17–1.92)
Urology, $n = 3{,}491$								
Never (43%)	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Prior (21%)	1.18 (0.70–1.99)	1.48 (0.90–2.45)	1.48 (0.81–2.71)	1.09 (0.63–1.86)	1.26 (0.85–1.86)	1.69 (1.15–2.49)	1.26 (0.68–2.34)	1.04 (0.77–1.41)
Current (36%)	1.23 (0.78–1.93)	1.97 (1.23–3.15)	1.37 (0.75–2.48)	1.27 (0.77–2.10)	1.57 (1.09–2.27)	1.44 (1.00–2.07)	1.16 (0.62–2.17)	1.19 (0.90–1.58)

Current current smoker within 1 year, *Prior* noncurrent smoker with > 0 recorded pack years of smoking, *Never* noncurrent smoker with 0 or missing recorded pack-years of smoking

Adjusted for fixed effects of age, race/ethnicity, work RVU, surgeon specialty, ASA classification, alcohol use, and year. SSI additionally adjusted for wound class. Models include a random effect for hospital when possible

Comparison of never smokers to current and prior smokers

- GI malignancies: prior and current smokers were more likely to have SSI, CPO (pneumonia, failure to wean form ventilator, reintubation), return to OR, 30 day and 1 year mortality
- Thoracic malignancies: current smokers were more likely to have CPO (pneumonia, failure to wean form ventilator, reintubation) and higher 1 year mortality
- Urologic malignancies: current smokers had elevated risk of CPO (pneumonia, failure to wean form ventilator, reintubation) and return to OR

Direct comparison of current smokers to prior smokers using prior smokers as a reference group

TABLE 4 Direct comparison of current smokers to prior smokers, using prior smokers as a reference group

Cancer site/Smoking status	Surgical site infection	Pneumonia	Failure to wean	Reintubation	Combined pulmonary outcome	Return to OR	30-day mortality	1-year mortality
GI, $n = 12{,}432$								
Never (49%)	0.80 (0.70–0.91)	0.66 (0.54–0.79)	0.63 (0.51–0.78)	0.60 (0.49–0.74)	0.62 (0.53–0.73)	0.84 (0.72–0.97)	0.67 (0.53–0.84)	0.82 (0.72–0.93)
Prior (25%)	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Current (26%)	0.96 (0.82–1.11)	1.30 (1.07–1.59)	1.40 (1.12–1.74)	1.30 (1.05–1.60)	1.22 (1.04–1.44)	1.10 (0.93–1.30)	0.94 (0.72–1.23)	1.33 (1.16–1.53)
Thoracic, $n = 4{,}490$								
Never (16%)	1.44 (0.79–2.62)	0.95 (0.69–1.31)	0.87 (0.57–1.31)	0.90 (0.62–1.30)	0.93 (0.70–1.23)	1.03 (0.72–1.47)	0.70 (0.43–1.14)	0.84 (0.65–1.09)
Prior (29%)	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Current (55%)	1.34 (0.83–2.18)	1.44 (1.15–1.81)	1.42 (1.06–1.90)	1.55 (1.19–2.01)	1.51 (1.23–1.85)	1.34 (1.03–1.74)	0.91 (0.64–1.30)	1.26 (1.05–1.52)
Urology, $n = 3{,}491$								
Never (43%)	0.85 (0.50–1.43)	0.67 (0.41–1.12)	0.68 (0.37–1.24)	0.92 (0.54–1.58)	0.79 (0.54–1.17)	0.59 (0.40–0.87)	0.79 (0.43–1.47)	0.96 (0.71–1.30)
Prior (21%)	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Current (36%)	1.04 (0.62–1.75)	1.33 (0.80–2.20)	0.92 (0.50–1.71)	1.17 (0.67–2.04)	1.25 (0.84–1.86)	0.85 (0.58–1.25)	0.92 (0.46–1.81)	1.14 (0.83–1.57)

Current current smoker within 1 year, *Prior* noncurrent smoker with > 0 recorded pack years of smoking, *Never* noncurrent smoker with 0 or missing recorded pack-years of smoking

Adjusted for fixed effects of age, race/ethnicity, work RVU, surgeon specialty, ASA classification, alcohol use, and year. SSI additionally adjusted for wound class. Models include a random effect for hospital when possible

Direct Comparison of current and prior smokers

- GI malignancies: current smokers were more likely to have CPO (pneumonia, failure to wean form ventilator, reintubation), and 1 year mortality
- Thoracic malignancies: current smokers were more likely to have CPO (pneumonia, failure to wean form ventilator, reintubation), return to OR and higher 1 year mortality
- Urologic malignancies: current smokers had similar risk of complications and mortality

Length of postsurgical stay

- Unadjusted: never smoker: 9.8 days; prior smoker:10.7 days; current smoker 10.6 days
- Adjusted: current smokers had a significant increase in length of stay compared with never smokers: 7.5% GI, 8.2% thoracic
- Adjusted: current smokers had a significant increase in length of stay compared with prior smokers: 4.7% GI, 9% thoracic

Conclusions

- Smoking has significantly increased the risk of postoperative complications and death in patients undergoing major cancer surgery in the VA
- We showed a significantly elevated risk of postoperative complications and death when directly comparing current to prior smokers with GI cancers and thoracic malignancies
- Consider smoking cessation interventions prior to all major cancer operations in the VA population to decrease risk of postoperative complication, mortality and prolonged surgical length of stay

Final conclusions

- The number of studies examining the perioperative impact of smoking cessation is limited
- Reduction in the quantity of cigarettes smoked does not result in the same effect as actual cessation
- An optimal period of preoperative smoking cessation can not be identified
- Preoperative smoking cessation for 4-8 weeks decreases pulmonary complications
- Preoperative smoking cessation for over 4 weeks may improve wound healing

Final conclusions

- The cost of additional hospitalization, utilization of care and the added expense of a smoking related complications is difficult to measure but considerable
- Prevention of surgical complications improves patient outcomes and reduces cost
- Pulmonary complications have been reported to be the most costly surgical complications adding an additional $52,000 to the cost of the surgical procedure

Kelly Clarkson

- “What doesn't kill you makes you stronger” might not apply to smoking

Acknowledgement

- Elizabeth Campagna, MS
- Dr Frederick Grover
- Dr Mary Hawn
- Dr William Henderson