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SCIENTIFIC ARTICLE

Relationship between cigarette smoking and the carbon monoxide concentration in the exhaled breath with perioperative respiratory complications

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KEYWORDS
Smoking;
CO exhaled;
Peri-operative;
Respiratory complications;
Laparoscopic cholecystectomy

Abstract
Background: The purpose of the current study was to determine the effects of preoperative cigarette smoking and the carbon monoxide level in the exhaled breath on perioperative respiratory complications in patients undergoing elective laparoscopic cholecystectomies.
Methods: One hundred and fifty two patients (smokers, Group S and non-smokers, Group NS), who underwent laparoscopic cholecystectomies under general anesthesia, were studied. Patients completed the Fagerstrom Test for Nicotine Dependence. The preoperative carbon monoxide level in the exhaled breath levels were determined using the piCO+ Smokerlyzer 12 h before surgery. Respiratory complications were recorded during induction of anesthesia, intraoperatively, during extubation, and in the recovery room.
Results: Statistically significant increases were noted in group S with respect to the incidence of hypoxia during induction of anesthesia, intraoperative bronchospasm, bronchodilator treatment intraoperatively, and bronchospasm during extubation. The carbon monoxide level in the exhaled breath and the Fagerstrom Test for Nicotine Dependence, and number of cigarettes smoked 12 h preoperatively were designated as covariates in the regression model. Logistic regression analysis of anesthetic induction showed that a 1 unit increase in the carbon monoxide level in the exhaled breath level was associated with a 1.16 fold increase in the risk of hypoxia (OR = 1.16; 95% CI 1.01–1.34; $p = 0.038$). Logistic regression analysis of the intraoperative course showed that a 1 unit increase in the number of cigarettes smoked 12 h preoperatively was associated with a 1.16 fold increase in the risk of bronchospasm (OR = 1.16; 95% CI 1.04–1.30; $p = 0.007$). While in the recovery room, a 1 unit increase in the Fagerstrom Test for Nicotine Dependence score resulted in a 1.73 fold increase in the risk of bronchospasm (OR = 1.73; 95% CI 1.04–2.88; $p = 0.036$).

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Conclusions: Cigarette smoking was shown to increase the incidence of intraoperative respiratory complications while under general anesthesia. Moreover, the estimated preoperative carbon monoxide level in the exhaled breath level may serve as an indicator of the potential risk of perioperative respiratory complications.

PALAVRAS-CHAVE
Tabagismo;
CO expirado;
Perioperatório;
Complicações respiratórias;
Coleistectomia laparoscópica

Relação entre consumo de tabaco e concentração de monóxido de carbono na expiração com complicações respiratórias perioperatórias

Resumo
Justificativa: O objetivo deste estudo foi determinar os efeitos do tabagismo pré-operatório e o nível de monóxido de carbono no ar expirado sobre complicações respiratórias perioperatórias em pacientes submetidos a colecistectomias laparoscópicas eletivas.
Métodos: No total, 152 pacientes (Grupo F: fumantes; Grupo NF: não-fumantes) submetidos a colecistectomias laparoscópicas sob anestesia geral foram avaliados. Os pacientes completaram o Teste para Dependência de Nicotina de Fagerstrom. Os níveis pré-operatórios de monóxido de carbono no ar expirado foram determinados usando o piCO + Smokerlyzer 12 h antes da cirurgia. As complicações respiratórias foram registradas durante a indução da anestesia, no intraoperatório, durante a extubação e na sala de recuperação.
Resultados: Aumentos estatisticamente significativos foram observados no Grupo F em relação à incidência de hipoxia durante a indução da anestesia, broncoespasmo intraoperatório, tratamento broncodilatador intraoperatório e broncoespasmo durante a extubação. O nível de monóxido de carbono no ar expirado, o Teste para Dependência de Nicotina de Fagerstrom e o número de cigarros fumados em 12 h no pré-operatório foram designados como covariáveis no modelo de regressão. A análise de regressão logística da indução anestésica mostrou que um aumento de uma unidade no nível de monóxido de carbono no ar expirado foi associado a um aumento de 1,16 vezes do risco de hipoxia (OR = 1,16; IC de 95% 1,01–1,34; p = 0,038). A análise de regressão logística do período intraoperatório mostrou que um aumento de uma unidade no número de cigarros fumados em 12 h no pré-operatório foi associado a um aumento de 1,16 vezes no risco de broncoespasmo (OR = 1,16; IC de 95% 1,04–1,30, p = 0,007). Enquanto na sala de recuperação, um aumento de uma unidade no escore do Teste para Dependência de Nicotina de Fagerstrom resultou em um aumento de 1,73 vezes no risco de broncoespasmo (OR = 1,73; IC de 95% 1,04–2,88; p = 0,036).
Conclusões: O tabagismo mostrou aumentar a incidência de complicações respiratórias intraoperatórias sob anestesia geral. Além disso, o nível estimado de monóxido de carbono no ar expirado no pré-operatório pode servir como um indicador do risco em potencial de complicações respiratórias perioperatórias.

Introduction

Cigarette smoking, one of the most serious health-threatening problems, is responsible for the increasing incidence of chronic disorders of the respiratory and circulatory systems.[1–4] It has been reported that the probabilities of small airway narrowing, chronic lung changes, and increased bronchial reactivity should be considered during administration of anesthesia in patients who smoke cigarettes.[5] In addition, postoperative pulmonary complications, such as pharyngitis, coughing, and apnea occur more frequently in smokers. The postoperative mortality rate is higher in smokers than non-smokers.[6–10] Pulmonary function, in particular, is affected by stimulation of the abdominal organs during laparoscopic cholecystectomy and gallbladder traction.[11]

There are a number of studies which have focused on the incidence of perioperative respiratory complications in patients who have discontinued or reduced cigarette smoking weeks before surgery.[4,7,8] Although the physiologic effects of long-term cessation of cigarette smoking before surgery are widely known, including the reduction in respiratory complications, the effects of preoperative cessation of smoking over a short period of time have not been thoroughly investigated.[12,13] A number of studies involving cigarette smoking have relied on self-reporting, and detailed smoking data have not been recorded in retrospective studies.[1,4,13] The estimated the carbon monoxide level in the exhaled breath e(BCO) level is a simple, non-invasive, rapid, and inexpensive technique that helps confirm the interval of non-smoking.[2–4,14,15]

In the current study we determined the relationships between perioperative respiratory complications during elective laparoscopic cholecystectomy, and preoperative cigarette smoking and the eBCO level.

Methods

Written informed consent was obtained from each patient. The study protocol was approved by the local Ethics Committee. The study was conducted in accordance with the principles of the Declaration of Helsinki. The work undertaken was a prospective and single blind investigation carried out in one center between December 2014 and May 2016 involving patients diagnosed with cholelithiasis who underwent elective laparoscopic cholecystectomies. The patients included in the study were 18–70 years of age, had a sustained smoking habit during the previous 6 months, an American Society of Anesthesiologists (ASA) score of I–II, and a Body Mass Index (BMI) < 30 $kg{\cdot}m^{-2}$. The exclusion criteria were strict to ensure the elimination of any cause other than sustained cigarette smoking that may affect the monitored respiratory functions, and included the following: a history of allergies to the medications to be used; respiratory infection during the previous 1 month; a known psychiatric disorder; chronic obstructive pulmonary disease; hepatic or renal insufficiency; coronary heart disease; restrictive and infliltrative lung diseases; anticipated entubation complications; and discontinued cigarette smoking during the 12 h prior to surgery. Patients who had not previously smoked tobacco products, including cigarettes, cigars, and pipes, but had been exposed at home or in the workplace to secondhand smoke, were designated as passive smokers and excluded from the study. Patients declining the procedure to estimate the eBCO level before induction of anesthesia were also excluded from the study.

The enrolled patients were grouped as smokers (Group S, $n = 75$) and non-smokers (Group NS, $n = 77$). The demographic details and cigarette smoking habits of all patients were queried and recorded. In Group S, the age at which the patient began smoking, the duration of the habit (in years), the number of cigarettes smoked per day, and whether or not the patient smoked cigarettes during the 12 h before surgery, and if so, the number of cigarettes smoked were also recorded. On the day of surgery, nicotine dependency was assessed by means of the Fagerstrom Test for Nicotine Dependence (FTND)[16] and the eBCO level was estimated using the piCO+ Smokerlyzer® (Bedfont Micro Breathalyzer; Kent, the United Kingdom) before induction of anesthesia.

The anesthesiologists were blinded and did not know the preoperative eBCO level or the FTND score. Midazolam (0.01–0.02 $mg.kg^{-1}$) was infused as a pre-medication, followed by i.v. propofol (2 $mg.kg^{-1}$), rocuronium (0.6 $mg.kg^{-1}$), and fentanyl (1–2 $mcg.kg^{-1}$) for induction of anesthesia. Sevoflurane in O_2+ air was used as maintenance anesthesia to achieve minimum alveolar concentration value of 1.0. Close to the termination of the intervention, i.v. metoclopramide HCl (10 mg) and i.v. acetaminophen (2 g) were administered. At the start of spontaneous respirations, extubation was carried out after reversal doses of i.v. neostigmine (0.03–0.05 $mg.kg^{-1}$) and atropine sulphate (0.01 $mg.kg^{-1}$).

Primary outcomes

All patients were routinely monitored and the following data were recorded: preoperative peripheral oxygen saturation (SpO_2); hypoxia at the time of induction; hypoxia, brochospasm, and bronchodilator treatment intraoperatively; bronchospasm and bronchodilator treatment at extubation; and hypoxia, bronchospasm, and the incidence of apnea, sore throat, headache, and coughing (including Grade 1) in the recovery room.[17] Hypoxia was defined as a $SpO_2 \leq 95\%$ for peripheral oxygen saturation in >1 min.

Secondary outcomes

The secondary outcomes included the following: the time elapsed from induction to extubation, which represented the period under general anesthesia; and the time required for complete recovery after extubation. The Modified Aldrete Score (MAS) was recorded 5, 10, and 15 min after admission to the recovery room. The MAS score upon satisfactory completion of post-operative recovery was recorded.

Statistical analysis

The Kolmogorov–Smirnov test was used to determine whether or not the variables are normally distributed. Continuous variables are described by the mean ± standard deviation or median (minimum:maximum) and categorical data are expressed as n (%). The Pearson chi-square and Fisher's exact tests were used to detect differences between groups on the basis of the categorical variables. An independent sample *t*-test was used to compare the following parameters in Groups S and NS: age; height; weight; duration of anesthesia; eBCO level. Mann–Whitney *U* test was performed to compare 5th minutes MAS scores and the difference between 15th and 5th, and also between 10th and 5th minutes MAS scores. Two way mixed ANOVA with repeated measurements was performed in order to examine the main effect of MAS measurements and the interaction of these main effects with the S and NS Groups. To determine risk factors affecting hypoxia and the development of bronchospasm in Group S, binary logistic regression analysis with a backward selection procedure was performed. The eBCO level, FTND, and the number of cigarettes smoked 12 h pre-operatively were selected as covariates in the regression models. A post hoc power analysis was performed based on the hypoxia proportions at induction (18.70% for Group S vs. 5.20% for Group NS). Using GPower 3.1 (http://www.gpower.hhu.de/), a power of 74% with an α of 0.05 were calculated when comparing the chi-square test with $n = 75$ for Group S and $n = 77$ for Group NS with effect size of $d = 0.19$. Statistical evaluation of the data were carried out using SPSS 21.0 for Windows (Statistical Package for the Social Sciences, Armonk, NY, USA) and a $p < 0.05$ indicated statistical significance.

Results

Of the 221 patients undergoing laparoscopic cholecystectomies, the data derived from 152 patients were included

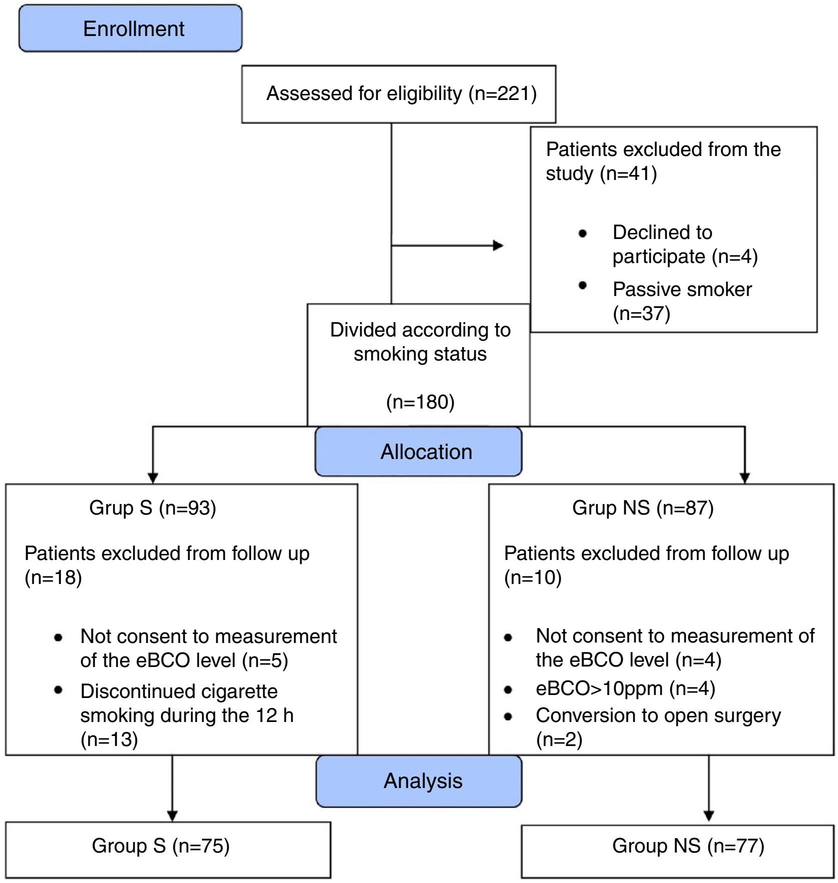

Figure 1 Flow chart of procedures.

in the study analysis. The data from the following patients were excluded: 37 passive smokers; 13 patients in Groups S who had stopped smoking during the 12 h before surgery; 5 patients in Group S and 4 patients in Group NS who did not consent to measurement of the eBCO level; 4 patients in Group NS with a eBCO level > 10 ppm, which was attributed to passive smoking; and 2 patients who underwent conversion to open cholecystectomies (Fig. 1).

The patient demographic data is shown in Table 1. There were no statistically significant differences between Groups S and NS ($p > 0.05$).

The details of the cigarette smoking habit data for the Group S patients are shown in Table 2. The mean FTND score was determined to represent a low-level dependency (3.76 ± 2.07).

Primary outcomes

No statistically significant intergroup differences were detected with respect to the data on pre-operative hypoxia, intraoperative hypoxia, bronchodilator treatment at the time of extubation, and the incidences of sore throat and headaches during the recovery period; however, hypoxia during induction, intraoperative bronchospasm, and bronchodilator treatment and bronchospasm at the time of extubation were significantly higher in Group S than Group NS. In addition, the incidences of hypoxia, apnea, and coughing during recovery were significantly higher in Group S than Group NS (Table 3).

Multivariable logistic regression analysis was used to determine the risk factors affecting hypoxia and development of bronchospasm in Group S, and the monitored outcomes as summarized in Tables 4 and 5, respectively. Based on the logistic regression models constructed for hypoxia, models are not significant for preoperative, intraoperative and recovery stages (respectively $p = 0.809$, $p = 0.882$ and $p = 0.070$) whereas model is significant for induction stage ($p = 0.047$) and thus results for preoperative, intraoperative and recovery stages could not be interpreted. A 1 unit increase in the eBCO level resulted in a 1.16 fold increase in the risk of hypoxia during anesthetic induction by logistic regression analysis (OR = 1.16; 95% CI 1.01–1.34; $p = 0.038$). Based on the development of bronchospasm during extubation logistic regression model, the results were not significantly different, and thus could not be interpreted. Based on the logistic regression models constructed for development of bronchospasm, model is not significant for extubation stage ($p = 0.082$) whereas models are significant for intraoperative and recovery stages (respectively $p = 0.005$ and $p = 0.019$) and thus results for extubation stage could not be interpreted. Based on logistic regression analysis, a 1 unit increase in the tabagism level led to a 1.16 fold increase in the risk of bronchospasm (OR = 1.16; 95% CI 1.04–1.30; $p = 0.007$). During the recovery stage, a 1 unit increase in the FTND score led to a 1.73 fold increase

Table 1 Demographic data.

Variable	Group S ($n = 75$)	Group NS ($n = 77$)	p-Value
Age (years)	43 ± 11.45	48.49 ± 12.15	0.059[a]
Height (cm)	167.12 ± 8.29	164.30 ± 9.49	0.610[a]
Body weight (kg)	77.76 ± 14.63	77.51 ± 12.96	0.910[a]
Female/male (%)	44 (58.70%)/31 (41.30%)	55 (71.40%)/22 (28.60%)	0.099[b]
Employed/unemployed/retired (%)	44.60%/40.50%/14.90%	27%/56.80%/16.20%	0.073[b]

Data were presented as mean ± standard deviation and n (%).
[a] Independent samples t-test.
[b] Pearson chi-square test.

Table 2 Cigarette smoking habits.

Baseline characteristics	Group S ($n = 75$)
Starting age of smoking (years)	19.80 ± 7.46
Cigarettes smoked per day	14.61 ± 8.94
Duration of smoking (years)	20.89 ± 11.93
Number of cigarettes smoked 12 h preoperative	5.45 ± 6.36
FTND	3.76 ± 2.07

Data were presented as mean ± standard deviation.
FTND, Fagerstrom Test for Nicotine Dependence.

in the risk of bronchospasm (OR = 1.73; 95% CI 1.04–2.88; $p = 0.036$).

Secondary outcomes

No statistically significant intergroup difference existed in the duration of surgery between the S and NS Groups ($p = 0.21$). The length of time under anesthesia was significantly longer for Group S than Group NS ($p = 0.048$). The length of time required for recovery was also significantly longer for Group S than Group NS ($p = 0.031$) (Table 6). The 5th minute MAS score was significantly higher in the NS Group ($p < 0.001$). The median MAS scores in the S and NS Groups were 9 (5:10) and 10 (7:10), respectively, at the 5th minute measurements, and the median increase in the MAS score was 2 (0:5) (0:3) and there was a difference between the two groups in terms of the increase amounts obtained according to the 5th minute measurement ($p < 0.001$). At the 15th minute, the median MAS scores in the N and NS Groups were 10 (8:10) and 10 (8:10), respectively, and the median increase in the MAS score in the S Group was 2 (0:7) (0:4) and there was a difference between the two groups in the increase amounts obtained according to the 5th minute measurement ($p < 0.001$) (Table 6). ANOVA analysis was performed to evaluate the changes in MAS parameter for both between serial measurements and for scores between groups. A one-way repeated measured analysis of variance (ANOVA) was conducted evaluate the null hyphotesis that there is no change in participants's MAS scores. The results of ANOVA indicated significant time effect, Wilks's Lambda = 0.35, $F(2, 149) = 137.94$, $p < 0.001$, $\eta^2 = 0.65$. Thus, there is significant evidence to reject the null hyphotesis. Post hoc tests using the Bonferroni correction revealed that each pairwise difference was significant (p-values for MAS 5th min. vs. MAS 10th min, MAS 5th min. vs. MAS 15th min. and MAS 10th min. vs. MAS 15th min. were $p < 0.001$). There was a significant increase in MAS scores over time (mean 5th MAS score was 8.10 ± 1.64, mean

Table 3 Comparison of the patients in Groups S and NS on the perioperative incidences of respiratory complications (n, %).

Stages of the surgery	Recorded complications	Group S ($n = 75$)	Group NS ($n = 77$)	p-Value
Preoperative	Hypoxia	9 (12%)	5 (6.50%)	0.241[a]
Induction	Hypoxia	14 (18.70%)	4 (5.20%)	0.010[a]
Intraoperative	Hypoxia	4 (5.30%)	2 (2.60%)	0.439[b]
	Bronchospasm	6 (80%)	0	0.013[b]
	Bronchodilator treatment	7 (9.30%)	1 (1.30%)	0.033[b]
Extubation	Bronchospasm	4 (5.30%)	0	0.057[b]
	Bronchodilator treatment	1 (1.30%)	0	0.493[b]
Recovery room	Hypoxia	27 (36%)	6 (7.80%)	<0.001[a]
	Apnea	5 (6.70%)	0	0.027[b]
	Sore throat	16 (21.30%)	9 (11.70%)	0.109[a]
	Headache	10 (13.30%)	4 (5.20%)	0.083[a]
	Coughing	31 (41.30%)	5 (6.50%)	<0.001[a]
	Bronchospasm	1 (1.30%)	0	0.493[b]

Data were presented as n (%).
[a] Pearson chi-square test.
[b] Fisher's exact test.

Table 4 Independent risk factors affecting hypoxia development.

Stages of the anesthesia	Factor	Wald	OR (95% CI)	*p*-Value
Preoperative	Tabagism	0.22	0.97 (0.84–1.12)	0.643
	E(BCO)	0.19	0.96 (0.79–1.17)	0.664
	FTND	0.57	1.15 (0.81–1.62)	0.450
Induction	Tabagism	0.73	0.95 (0.85–1.07)	0.393
	E(BCO)	4.32	1.16 (1.01–1.34)	0.038
	FTND	0.35	0.90 (0.65–1.26)	0.553
Intraoperative	Tabagism	0.07	1.02 (0.88–1.18)	0.798
	E(BCO)	0.26	1.06 (0.86–1.31)	0.609
	FTND	0.47	0.82 (0.45–1.47)	0.495
Recovery room	Tabagism.	4.38	0.88 (0.77–0.99)	0.036
	E(BCO)	0.01	1.09 (0.84–1.40)	0.943
	FTND	0.38	1.09 (0.85–1.39)	0.537

E(BCO), carbon monoxide level in the exhaled breath; FTND, Fagerstrom Test for Nicotine Dependence; Tabagism, number of cigarettes smoked in the 12 h before surgery.

Logistic regression models are not significant for preoperative, intraoperative and recovery stages (respectively $p = 0.809$, $p = 0.882$ and $p = 0.070$) whereas model is significant for induction stage ($p = 0.047$).

Table 5 Independent risk factors affecting bronchospasm development.

Stages of the anesthesia	Factor	Wald	OR (95% CI)	*p*-Value
Extubation	Tabagism	3.43	1.12 (0.99–1.25)	0.067
	E(BCO)	0.18	0.94 (0.71–1.25)	0.663
	FTND	0.01	1.02 (0.60–1.76)	0.937
Intraoperative	Tabagism	7.39	1.16 (1.04–1.30)	0.007
	E(BCO)	0.25	1.05 (0.87–1.27)	0.616
	FTND	0.47	0.84 (0.50–1.40)	0.492
Recovery room	Tabagism	0.13	0.69 (0.42–1.14)	0.151
	E(BCO)	0.64	1.05 (0.86–1.29)	0.642
	FTND	4.40	1.73 (1.04–2.88)	0.036

E(BCO), carbon monoxide level in the exhaled breath; FTND, Fagerstrom Test for Nicotine Dependence; Tabagism, number of cigarettes smoked in the 12 h before surgery.

Logistic regression model is not significant for extubation stage ($p = 0.082$) whereas models are significant for intraoperative and recovery stages (respectively $p = 0.005$ and $p = 0.019$).

Table 6 Comparison of MAS scores and eBCO among groups.

	Group S ($n = 75$)	Group NS ($n = 77$)	*p*-Value
Duration of anesthesia (min)	77.50 (30–190)	70 (40–170)	0.048[b]
Duration of surgery (min)	60 (20–180)	55 (30–160)	0.213[b]
Time required for recovery (min)	20 (16–60)	15 (10–45)	0.031[b]
MAS (5th minute)	7 (1–10)	9 (6–10)	<0.001[b]
MAS (10–5th minute)	2 (0–5)	1 (0–3)	<0.001[b]
MAS (15–5th minute)	2 (0–7)	1 (0–4)	<0.001[b]
eBCO	7.50 ± 4.66	2.53 ± 1.22	<0.001[a]

MAS, The Modified Aldrete Score; e(BCO), carbon monoxide level in the exhaled breath; Min, minute; 10–5th, difference score of MAS measurement between 10th and 5th minutes; 15–5th, difference score of MAS measurement between 15th and 5th minutes.

Data were presented as mean ± standard deviation and median (minimum:maximum).

[a] Independent samples *t*-test.

[b] Mann–Whitney *U* test.

10th MAS score was 9.36 ± 1.86 and mean 15th MAS score was 9.89 ± 0.37). There was significant main effect of MAS measurements overall ($p < 0.001$) and there was significant interaction effect between MAS and study groups so it can be concluded that the difference between measurements depends on group membership ($p < 0.001$). The separate effects of MAS for Group S and Group NS would be obscured by taking them together so S and NS Groups were separately (simple effects) analyzed instead. For Group S analysis MAS has an effect for respondents Wilks's Lambda = 0.27, $F(2, 73) = 97.72$, $p < 0.001$, $\eta^2 = 0.76$. Post hoc tests using the Bonferroni correction revealed that each pairwise difference was significant (p-values for MAS 5th min. vs. MAS 10th min, MAS 5th min. vs. MAS 15th min. and MAS 10th min. vs. MAS 15th min. were $p < 0.001$). There was a significant increase in MAS scores over time (mean 5th MAS score was 7.25 ± 1.73, mean 10th MAS score was 9.09 ± 1.04 and mean 15th MAS score was 9.83 ± 0.45). For Group NS analysis MAS has an also effect for respondents Wilks's Lambda = 0.50, $F(2, 75) = 37.95$, $p < 0.001$, $\eta^2 = 0.50$. Post hoc tests using the Bonferroni correction revealed that each pairwise difference was significant (p-values for MAS 5th min. vs. MAS 10th min, MAS 5th min. vs. MAS 15th min. and MAS 10th min. vs. MAS 15th min. were $p < 0.001$). There was a significant increase in MASS scores over time (mean 5th MAS score was 8.92 ± 1.04, mean 10th MAS score was 9.69 ± 0.59 and mean 15th MAS score was 9.96 ± 0.25). The preoperative eBCO levels in Group S were significantly higher compared to Group NS (7.50 ± 4.66 ppm vs. 2.53 ± 1.22 ppm, respectively; $p < 0.001$) (Table 6).

Discussion

The relationship between preoperative eBCO levels and the effects of cigarette smoking on perioperative respiratory complications was the focus of the current study. In the Group S patients, the incidences of the following were significantly increased: hypoxia during anesthetic induction; intraoperative bronchospasm and bronchodilator treatment; bronchospam at the time of extubation; hypoxia, coughing, and apnea in the recovery room; and the time required for recovery.

Higher incidences of perioperative complications, such as increased reactivity of the respiratory system, sore throat, coughing, and apnea, have been reported in patients who smoke cigarettes.[1,4–10] Our findings are in agreement with the extant literature.

Although the time taken to complete the surgery did not differ significantly between the patients in Groups S and NS, the time under general anesthesia was significantly prolonged in the Group S patients. The reported duration of laparoscopic cholecystectomies has been reported to range between 30 and 166 min,[3–6] which is in agreement with our findings. The duration of anesthesia has been reported to persist 3.5–4.5 h, and has generally been based on group comparisons.[5,18] Lee et al.[18] compared smokers and non-smokers who underwent different surgeries, and did not demonstrate a significant difference in duration of anesthesia, whereas the time under anesthesia in Group S was significantly prolonged in the current study. But the clinical significance of some minutes to awake is minimal, and this could not be considered a valid outcome.

Several studies have reported the eBCO level in smokers to range between 11 and 15.5 ppm.[4,6,15] The mean eBCO for smokers in the current study was 7 ppm. Only one study has reported the relationship between the eBCO level and the incidence of respiratory complications.[19] In the current study, the data on smoking and not smoking within 12 h before surgery were used to determine the correlations with respiratory complications; data on passive smokers were not included in the evaluation.

The mean FTND score in the current study was consistent with a low level of nicotine dependence. The FTND score has been used to estimate the magnitude and profile of nicotine dependence.[3,6] Moller et al.[3] reported a moderate level of dependency in most of the patients in their study, while the mean FTND score reported by Lee et al.[6] was 4.3. In the majority of studies involving the effects of cigarette smoking on surgical outcomes, the magnitude of nicotine dependency was not investigated.[1,3,13,18]

The current study was limited to patients without systemic medical conditions and required laparoscopic cholecystectomies. Hence, the data are more uniform compared to previous studies involving the effects of cigarette smoking on perioperative respiratory complications with data collected from diverse surgical and anesthetic procedures.[3–6,10,15,20] In addition, some of the studies included smokers with cardiovascular and respiratory disorders, unlike the current study.[5,13]

Most studies have reported an elevated incidence of respiratory complications in patients with a sustained habit of cigarette smoking.[4–6,10] In the current study we demonstrated a higher incidence of respiratory complications in the Group S patients. Some of the reported studies have evaluated the intra- and post-operative complications separately,[4–6,18] while other studies have focused only on the postoperative complications.[3,7,10,15,21] We monitored the study patients for respiratory complications during the induction of anesthesia, intraoperatively, at the time of extubation, and during recovery. Respiratory complications occurred in 25.3% of the Group S patients and 3.9% of the Group NS patients while in the operating room, indicating an approximately 6 fold increase attributable to cigarette smoking. Inclusion of the respiratory complication data within the recovery room increased the incidence of complications 5 fold; specifically, respiratory complications affected 58.7% and 13% of the Group S and NS patients, respectively. The perioperative respiratory complication incidence reported by Lee et al.[18] was 9.5%. Myless et al.[4] reported an peri-operative respiratory complication incidence of 32.8% in cigarette smoking patients, which was 1.7 fold higher than non-smokers. Use of general anesthesia and performing upper abdominal surgery in proximity to the diaphragm may have contributed to the effects on the respiratory system and the presence of mild coughing in the recovery room, as reported here in. We observed an 18% incidence of hypoxia during induction in the Group S patients, which was 3 fold higher than the Group NS patients. An elevated BMI is known to complicate mask ventilation.[21] The mean value of BMI > 27 $kg \cdot m^{-2}$ in our patients may have contributed to the increased incidence of hypoxia together with cigarette smoking. Dennis et al.[19] reported a 2.2 fold higher

Table 7 The studies of perioperative respiratory complications related to smoking.

Source	Study design	Period	Respiratuvar complications	Validation	Nicotine dependency	Type of surgery
Graybill et al.[1]	Retrospective	30 day postsurgey	Hypoxia Coughing Respiratory failure-infection	None	FTND	Laparoscopic gynecology
Moller et al.[3]	Randomized controled trial	During hospital stay	Respiratuar complications	CO reading	FTND	Orthopedic
Myles et al.[4]	Cohort prospective	İntraope Uyanma 7 day postsurgey	Hypoxia Bronchospasm Laringospasm Coughing Apne	CO reading	None	Ambulatory surgery
Sakai et al.[5]	Retrospective	Intraoperative Recovery Postoperative	Hypoxia Bronchospasm	None	None	Abdominal surgery
Schwilk et al.[13]	Retrospective	Perioperative	Bronchospasm	CO reading	FTND	Orthopedic
Lee et al.[18]	Prospective	Intraoperative Recovery Pacu Postoperative	Hypoxia Bronchospasm Coughing	Uriner cotinin	FTND	Urological Orthopedic Cardiac General
Lindström et al.[15]	Randomized controled trial	30 day postsurgery	Hypoxia Bronchospasm Bronchodilator need	CO reading	FTND	General Orthopedic
Warner et al.[22]	Retrospective	Perioperative 30 day postsurgery	Bronchospasm Bronchodilator need	None	None	General Urology Cardiology Gynecology

CO, carbon monoxide; FTND, Fagerstrom Test for Nicotine Dependence; Pacu, postoperative care unit.

incidence of hypoxia during anesthesia induction in passive smokers compared to non-smokers. In patients with elevated carboxyhaemoglobin levels, but without data on smoking status, the decline in SpO_2% during anesthesia induction was more pronounced than other complications.[19] The perioperative respiratory complications related to smoking in several studies are summarized in Table 7.

In the current study, the intraoperative incidences of bronchospasm and bronchodilator treatment were 8% and 9.3%, respectively, reflecting significantly increased respiratory complications in Group S patients. Our results are in agreement with the findings of Myles et al.,[4] who reported the incidence of intraoperative and post-anesthetic care unit bronchospam and laryngospam to be 9.4% nit. The incidence of intraoperative bronchospam was 5% among cigarette smoking patients, as reported by Lee et al.[18] Indeed, this result is lower than that determined in our study, and may be due the inclusion of orthopedic, general, gynecologic and urologic cases in their study groups.[4,18] Warner et al.[22] reported the perioperative incidence of bronchospasm as 2.2% in their retrospective study. The reason for the lower incidence of bronchospasm than recorded in our study may be due to the predominance of non-smoking patients and approximately 40% of the cases did not have upper abdominal surgery. In a retrospective study, Schwilk et al.[13] reported a 2% incidence of perioperative bronchospasm among cigarette smokers with different ASA scores and undergoing orthopedic surgical procedures. In another retrospective study, Sakai et al.[5] reported significantly increased incidences of hypoxia intraoperatively and during recovery among patients with respiratory and cardiac problems, which is similar to our observations.

The incidence of hypoxia in the recovery room has been reported to range between 1% and 9.4%.[4,5,18] By way of comparison, the incidence of hypoxia in Group S patients was 36%, which was much higher than the results of the aboveforementioned studies. The estimated $SpO_2 < 90-92\%$ in these studies may partly underlie the lower incidence of hypoxia compared to the current study.

We have noted a 41.3% and 6.5% incidence of coughing among the smoking and non-smoking patients, respectively, indicating a significant difference between the two groups in the recovery room. In studies which have reported the incidences of coughing among smokers and non-smokers, the values ranged between 1.7—20% and 0.3—11%, respectively.[4,18] The higher results obtained in our study may have been due to our differentiation between mild and severe coughing, as well as inclusion of patients undergoing an upper abdominal surgical procedure only.

We recorded a significantly elevated incidence of apnea (6.7%) during the recovery period in the Group S patients. In the study conducted by Myles et al.,[4] the incidence of apnea among smokers over 7 days post-operatively was 6.8%, which is consistent with our results.

With respect to the published reports on the effect of cigarette smoking on the peri-operative respiratory complications, we have not identified data on MAS scores in adults. Also, some studies have not included the time required for recovery.[3,6,10] In the current study, the time required for recovery was significantly longer in the Group S patients. Neto et al.[23] reported results that are in agreement with the results reported herein, whereas Graybill et al.[1] did not find a significant difference between smokers and non-smokers. Although our results on awakening in the recovery room were significantly different between the two groups, the time taken to awaken did not result in any significant clinical changes.

The limitations to our study include the low FNDT scores, the lack of an objective scale on the severity of coughing, and the absence of data on long-term respiratory complications.

Summary

The current study is the first to evaluate the respiratory complications associated with laparoscopic cholecystectomy at each stage of the procedure, including anesthesia induction, the intraoperative period, the extubation stage, and the recovery period. We believe that we have contributed to the general literature by reporting the increased incidence of perioperative respiratory system complications during elective laparoscopic cholecystectomies among patients with a sustained cigarette smoking habit. Specifically, the number of cigarettes smoked in the 12 h before surgery, the pre-operative eBCO level, and the FNDT score were shown to impact peri-operative respiratory complications.

It should be kept in mind that detailed queries on the preoperative cigarette smoking status of patients and measurement of the eBCO level using a simple and non-invasive technique would be useful for anesthesiologists with respect to the probability of perioperative respiratory complications. It has been shown here in that further research is warranted.

Conflicts of interest

The authors declare no conflicts of interest.

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