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ORIGINAL RESEARCH

The Effect of Passive Smoking on Early Clinical Outcomes After Total Knee Arthroplasty Among Female Patients

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Purpose: The aim of this study was to assess whether passive smoking affects clinical outcomes among female patients with knee osteoarthritis after being treated with total knee arthroplasty (TKA).

Methods: The study prospectively enrolled 216 female patients who did not smoke and those patients were classified into three groups in terms of the severity of exposure to environmental tobacco smoke. A three-month follow-up was conducted to assess the physical and mental outcomes between the three groups. The physical outcomes were evaluated by the visual analogue score (VAS), range of motion (ROM), hospital for special surgery (HSS) knee score, and postoperative complications. The mental outcomes were assessed by the anxiety and depression scale (HADS) and medical outcome study short form 36 (SF-36). Subgroup analysis of patients with and without surgical site infection (SSI) was also calculated.

Results: Baseline characteristics were similarly distributed between the three groups (P>0.05). Patients in the heavy passive smoking group had a higher VAS and a lower ROM score as compared with patients in the no and mild passive smoking group at discharge (P<0.01), 1 month (P<0.01), and 3 months (P<0.01) after surgery. Patients in the heavy passive smoking group also had a higher rate of HADS more than 8 at postoperative 1 month (P=0.01) and 3 months (P=0.03) and lower SF-36 summary (P<0.01) and HSS score (P<0.01) at postoperative 3 months. Forty-five postoperative complication events were observed during follow-up. Patients in the heavy passive smoking group (8.51%) had the highest SSI rate, followed by patients in the mild (1.82%) and no passive smoking group (0.88%) at discharge (P=0.02) and postoperative 1 month (P=0.03).

Conclusion: Passive smoking negatively affects TKA among female patients. It may trigger poor pain and functional outcomes, aggravate depression and anxiety, and deteriorate quality of life after discharge from hospital. Avoiding exposure to smoking environment may be beneficial among TKA female patients before and after surgery.

Keywords: passive smoking, knee arthroplasty, female patients, surgical site infection

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Introduction

Knee osteoarthritis has become a serious public health problem due to a growing aging population, which usually contributes to knee pain and even disability among elderly female patients. Regarding all therapeutic strategies, total knee arthroplasty (TKA) is a first line method to treat its advanced stage, since TKA is considered as an effective operation for the multitude of patients to alleviate pain and recover

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knee function.[1] However, there is a significant portion of unsatisfied patients, because postoperative complications remain a major concern. Studies have shown that the overall postoperative complication rate was up to 18.00–52.00%[2] and 2.82–6.00% of patients developed postoperative surgical site infection (SSI) after TKA.[3] Postoperative complications intensified economic burden and the average health cost was even double for SSI versus non-SSI patients after arthroplasty.[4]

Previous studies have shown that smoking was an important risk factor for predicting revision and postoperative complications among patients being treated with TKA.[5–7] Smoking negatively affected wound healing and was associated with increased soft tissue complications[8] due to vasoconstriction resulted from impaired oxygen transport and cellular metabolism.[9,10] Nicotine and byproducts of smoking were the culprits. Passive smoking also shows negative impacts on patients undergoing surgery.[11] Notably, passive smoking may even do more harm compared with active smoking.[12] However, the effects of passive smoking on clinical outcomes after TKA have not been widely elucidated. Studies have shown that the majority of the patients undergoing TKA were aged female.[1] In addition, active smokers in females only account for a percentage of 3.50%, while passive smokers were responsible for a high percentage of 54.60%, thus aged women were more easily vulnerable to live with the detrimental effects of passive smoking.[13,14]

Therefore, the purpose of this study aimed to evaluate the effects of passive smoking on prognosis after TKA. We speculated that passive smoking had a negative impact on clinical outcomes after TKA among female patients. Besides, we also analyzed the ability of a series of preoperative risk factors for predicting postoperative SSI.

Patients and Methods

Patients

We prospectively collected the clinical data of patients who were scheduled to undergo TKA due to knee osteoarthritis from September 2015 to June 2017 at the Department of Orthopedics in Chinese PLA General Hospital. Inclusive criteria were as follows: (1) female patients; (2) patients with an age of more than 50 years; (3) no smoking habit or exceed-ten-year smoking cessation. Participants were excluded if she (1) was diagnosed with severe physical or mental disease, (2) lived with family members whose smoking habit changed significantly, (3) failed to record time of exposure to smoke, and (4) was reluctant to participate in. The patient's flowchart is shown in Figure 1. We performed a chart review of both paper and electronic medical records for all patients by using standardized data collection forms and protocols. This study was approved by the Medical Research Ethics Board of Hainan Hospital of Chinese PLA General Hospital (No.301HNFY51) and informed written consents were obtained from all participated patients. This study was consistent with the Declaration of Helsinki.

Surgical Technique

Patients were operated on by experienced specialists under general anesthesia. Patients were routinely administered with antibiotics (ceftriaxone or vancomycin) prophylactically before the skin incision. The tourniquet was performed during the surgery. The operative procedures were routine and prosthesis (Gemini, MK-II. Link) was applied in each case. The incision was closed using continuous sutures for the deep layers, interrupted sutures for subcutaneous tissues, and staples for the skin. Generally, we removed the drainage tube on the first postoperative day. The antibiotic therapy, thromboprophylaxis, and analgesia were routinely administered after the surgery. Postoperative rehabilitation was routinely performed the first day after surgery. Early ambulation was defined that any partial or full weight-bearing activities were achieved within 24 h under the supervision of a physiotherapist.[15]

Patient's Classification of Passive Smoking

This study divided enrolled patients into three groups in terms of the severity of exposure to environmental tobacco smoke: no, mild, and heavy passive smoking groups. Passive smoking was defined that patients were exposed to smoking in the participant's family or presented at the workplace. Passive smoking day (PSD) was used to measure the severity of passive smoking.[16] We recorded the time of exposure to cigarette smoke for three months after discharge. The patients were classified into three different groups according to the PSD per week. In detail, no passive smoking group had a PSD of less than 1 day (at least 15-minute exposure per day) per week, mild passive smoking group had a PSD of more than 1 day but less than 3 days per week, and heavy passive smoking group had a PSD of more than 3 days per week.

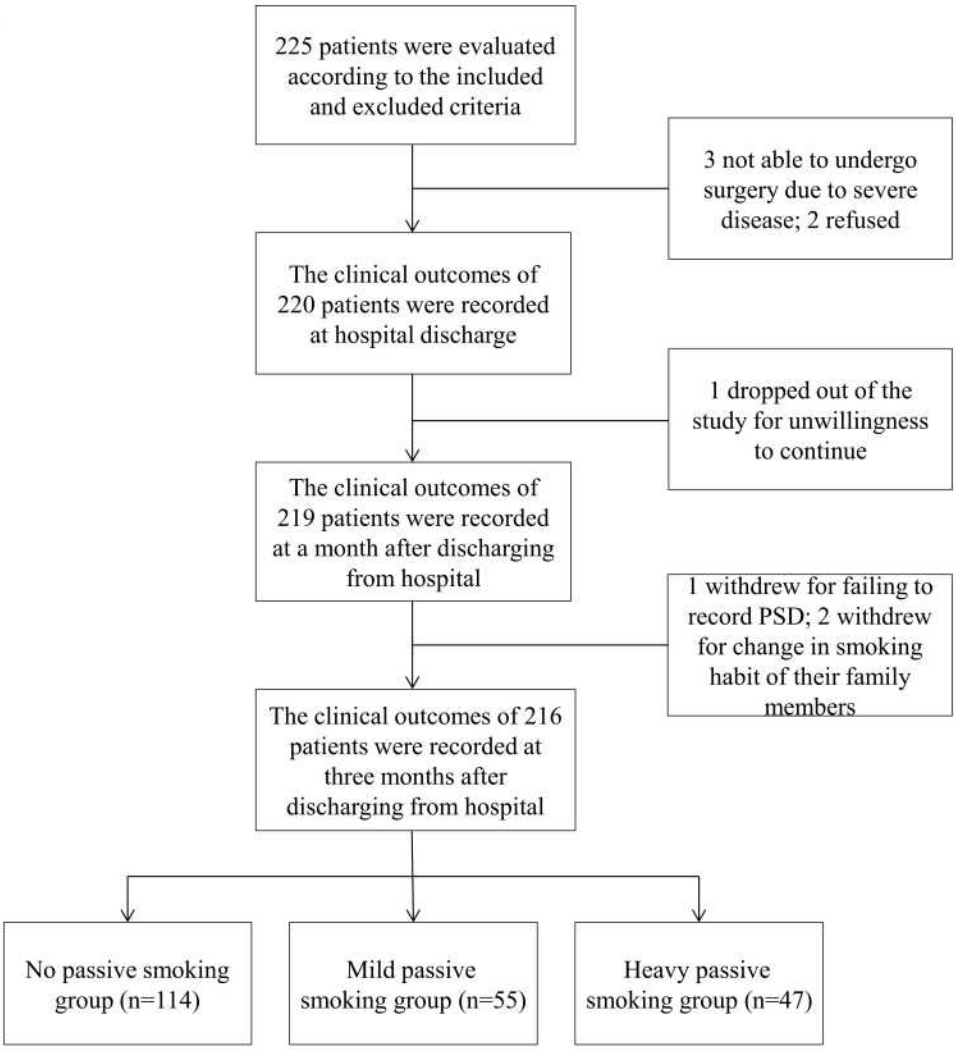

Figure 1 Patient's flowchart.

Demographic Data and Corresponding Definitions

We recorded basic demographic information in the three groups, including age, Body Mass Index (BMI), American Society of Anesthesiologist (ASA) score, preoperative comorbidities (including cardiovascular, respiratory or diabetic disease, and neurological disease), preoperative pain level, preoperative knee function level, the Hospital for Special Surgery (HSS) knee score, anxiety and depression, and the quality of life.

The visual analogue score (VAS) was used to evaluate pain levels. The active range of motion (ROM) which means the maximum range patients can reach without physicians' help was measured using a goniometer by surgeons to evaluate knee function level. HSS knee score was widely used to assess the results of arthroplasty and osteoarthritis symptoms.[17] The Hospital Anxiety and Depression Scale (HADS) was used to assess mental symptoms of patients. In detail, the HADS is a 14-item self-report questionnaire that includes the anxiety subscale (7 items) and the depression subscale (7 items). HADS scores of 8 or more on each subscale were considered significant.[18] The quality of life was assessed with the Medical Outcome Study Short Form 36 (SF-36). We calculated the physical component summary (PCS) and the mental component summary (MCS) and the score ranged from 0 to 100 with higher scores representing better quality of life.[19]

Observation Outcomes

Length of hospitalization, duration of surgery, and charges in the hospital were collected and compared between the

three groups. The pain score, ROM, HADS were evaluated before surgery, at discharge, and postoperative 1 and 3 months. As the follow-up time was limited to early-stage after the operation, HSS score and the quality of life were only assessed at three months after surgery. Questionnaires included HADS, HSS, and SF-36, which were completed through a personal interview or a telephone interview.

Postoperative complications were recorded at discharge, 1, and 3 months after surgery. The complications included cardiovascular diseases, pulmonary diseases, deep venous thrombosis (DVT), surgical site infection (SSI), and neuropathies. The complications concerning other systems or organs were diagnosed and treated by corresponding specialists. SSI included the superficial incisional SSI, deep incisional SSI, and organ/space SSI. The diagnosis of SSI was conducted according to the criterion of the Centers for Disease Control (CDC).[8] We observed and recorded wound conditions, including skin temperature, hematoma, and fluid exudation. If a SSI was suspected, samples were obtained for the culture of bacteria. Any complications that occurred in the study were recorded in detail.

The patients were then divided into two subgroups and there were SSI patients and patients without SSI. The length of hospitalization, charges in hospital, VAS, ROM, HADS, and SF-36 Summary Scores were compared between the two groups.

Potential Postoperative SSI Predictors

Potential risk factors for postoperative SSI were identified based on a review of the literature and characteristics available from paper or electronic medical records. In the study, 14 characteristics, including age (years), BMI (kg/m^2), duration of surgery (min), ASA score (1 vs 2 vs 3), chronic heart diseases (yes vs no), chronic lung diseases (yes vs no), diabetic disease (yes vs no), neurological disease (yes vs no), preoperative VAS, preoperative ROM (°), preoperative HSS scores, preoperative HADS (≤8 vs >8), preoperative SF-36 summary Scores, and passive smoking status (no vs mild vs heavy) were analyzed for postoperative SSI.

Statistics

We used the Chi-square test to test differences in proportions and the Student's *t*-test, one-way ANOVA (Analysis of Variance) test, Kruskal–Wallis test, and analyses of variance with repeated measurement design to analyze continuous variables in order to appraise statistical discrepancy between the three groups. The logistic regression model was used to analyze the ability of risk factors for predicting postoperative SSI. Discrimination of the model was evaluated by the area under the receiver operating characteristic curve (AUROC). Calibration was assessed by using the Hosmer-Lemeshow goodness-of-fit test and a P-value of the test more than 0.05 indicates that there is no evidence of a lack of fit in the model. All data distribution was checked for the normality and homogeneity of the variances according to the Kolmogorov–Smirnov test and Levene's test. P<0.05 was defined as a significant difference. All P values were two-sided. SAS software (version 9.2) was used for all statistical analysis.

Results

Patient's Demographics

In the study, 216 female patients were enrolled. The mean age was 66.05±7.80 years, and the mean BMI was 28.82 ±5.04 kg/m^2, which indicates that the majority of patients were overweight or obese. In the entire cohort, 132 patients (61.11%) had an ASA score of 2, and 39 patients (18.06%) had chronic heart diseases. As for the quality of life before surgery, the physical component of the SF-36 summary score was 33.27±4.83 and the mental component was 40.51±10.90 (Table 1). Table 1 also showed that the difference of all preoperative variables was not significant between the three groups, which indicated that the distribution of characteristics was similar between the three groups.

Comparison of Outcomes Between the Three Groups

The difference of VAS was significant between the three groups at discharge (no passive smoking group: 2.82±1.42 vs mild passive smoking group: 3.24±1.35 vs heavy passive smoking group: 3.91±1.60, P<0.01, Table 2 and Figure 2), postoperative 1 month (no: 1.54±1.19 vs mild: 1.95±1.21 vs heavy: 2.06±0.87, P=0.01), and postoperative 3 months (no: 0.88±0.58 vs mild: 1.15±0.49 vs heavy: 1.34±0.64, P<0.01). Patients in the no passive smoking group had higher ROM scores as compared with patients in the heavy and mild passive smoking group at discharge (P<0.01, Table 2 and Figure 2), 1 month (P<0.01), and 3 months (P<0.01) after surgery. Patients in the no passive smoking group also had a lower rate of HADS more than 8 at postoperative 1 month (P=0.01, Figure 3) and 3 months (P=0.03), higher SF-36 summary scores at postoperative 3 months (P<0.01), and higher HSS score at postoperative 3 months (P<0.01), as compared with patients in the mild and heavy passive smoking group.

Table 1 Patient's Demographics

Variables	Patients (n=216)	Groups			P value
		No (n=114)	Mild (n=55)	Heavy (n=47)	
Age (years)	66.05±7.80	66.32±8.24	64.69±6.52	66.96±8.02	0.16
BMI (kg/m^2)	28.82±5.04	29.55±5.02	28.11±4.30	27.87±5.69	0.08
ASA score (%)					
1 (Healthy)	60	34 (29.8%)	14 (25.5%)	12 (25.5%)	0.92
2 (Minimally ill)	132	67 (58.8%)	36 (65.5%)	29 (61.7%)	
3 (Moderately ill)	24	13 (11.4%)	5 (9.1%)	6 (12.8%)	
Comorbidities					
Chronic heart diseases	39	17 (15%)	9 (16.3%)	9 (19.1%)	0.80
Chronic lung diseases	25	11 (9.6%)	6 (10.9%)	8 (17%)	0.41
Diabetes mellitus	16	7 (6.1%)	5 (9.1%)	4 (8.5%)	0.75
Neuropathies	9	5 (4.4%)	2 (3.6%)	2 (4.2%)	0.97
Preoperative VAS	4.14±0.92	4.25±0.82	4.09±1.02	3.94±1.00	0.12
Preoperative ROM (°)	104.64±13.80	105.72±14.57	105.49±14.93	101.04±9.45	0.17
Preoperative HSS scores	56.27±16.31	55.18±16.51	58.96±16.73	55.74±15.30	0.36
Preoperative HADS (>8)	42	19 (16.6%)	11 (20%)	12 (25%)	0.43
Preoperative SF-36 summary scores					
Physical Component	33.27±4.83	33.12±5.17	33.84±4.28	32.96±4.65	0.81
Mental Component	40.51±10.90	40.96±13.75	39.71±6.47	40.38±6.36	0.78

Abbreviations: BMI, body mass index; ASA, American Society of Anesthesiologists; VAS, visual analogue score; ROM, range of motion; HADS, hospital anxiety and depression scale; HSS, hospital for special surgery.

However, the length of hospitalization (P=0.41), duration of surgery (P=0.19), and charges in hospital (P=0.59) were not significantly different between the three groups. Considering complication, the rates in the heavy smoking group were the highest at discharge, postoperative 1 month, and 3 months, as compared with other two groups. The statistical analyses of the rates at discharge (P=0.06) and postoperative 1 month (P=0.08) almost reached significance. When patients in the mild passive smoking group were excluded in the analysis, patients in the no passive smoking group had a lower complication rate at discharge (P=0.03), postoperative 1 month (P=0.06), and 3 months (P=0.14), as compared with patients in the heavy smoking group (Figure 3). More details are shown in Table 2.

Comparison of Postoperative Complications Between the Three Groups

Forty-five postoperative complication events were observed during follow-up (Table 3). In detail, 25 complication events occurred at discharge, 13 complication events were observed at postoperative 1 month, and 7 complication events were recorded at postoperative 3 months. The most common complication was pulmonary diseases (6.48%, 14/216), followed by cardiovascular diseases (5.56%, 12/216) and SSI (5.56%, 12/216). Regarding the therapeutic strategies on SSI, all SSI patients received antibiotics for wound infections, 6 patients needed wound washouts, and 3 patients underwent one or two stage revisions.

Notably, patients in the heavy passive smoking group (8.51%) had the highest SSI rate, followed by patients in the mild passive smoking group (1.82%) and then the no passive smoking group (0.88%) at discharge (P=0.02). The similar result was observed at postoperative 1 month (P=0.03).

Subgroup Analysis of Patients with and without SSI

Subgroup analysis of patients showed that patients with SSI had a longer length of hospitalization (P<0.01, Table 4), higher charges in hospital (P<0.01), higher VAS at

Table 2 Comparisons of the Intraoperative Parameters and Postoperative Clinical Outcomes Between the Three Groups

Variables		No (n=114)	Mild (n=55)	Heavy (n=47)	P value
Length of hospitalization (days)		12.13±4.46	12.16±4.29	13.11±3.59	0.41
Duration of surgery (min)		107.83±8.44	107.93±7.74	110.17±4.96	0.19
Charges in hospital ($)		9758.54 ±383.08	9780.47 ±323.77	9820.57 ±269.52	0.59
VAS	Discharge	2.82±1.42	3.24±1.35	3.91±1.60	<0.01
	Postoperative 1 month	1.54±1.19	1.95±1.21	2.06±0.87	0.01
	Postoperative 3 months	0.88±0.58	1.15±0.49	1.34±0.64	<0.01
ROM (°)	Discharge	80.67±2.60	80.25±2.39	77.13±2.19	<0.01
	Postoperative 1 month	104.11±5.73	99.09±2.50	96.04±2.26	<0.01
	Postoperative 3 months	113.31±10.81	111.44±7.32	108.30±9.59	<0.01
HADS	Discharge (>8, %)	16 (14.04%)	9 (16.36%)	10 (21.28%)	0.53
	Postoperative 1 month (>8, %)	7 (6.14%)	10 (18.18%)	10 (21.28%)	0.01
	Postoperative 3 months (>8, %)	5 (4.39%)	7 (12.73%)	8 (17.02%)	0.03
Complications	Discharge (%)	10 (8.77%)	5 (9.09%)	10 (21.28%)	0.06
	Postoperative 1 month (%)	4 (3.51%)	3 (5.45%)	6 (12.77%)	0.08
	Postoperative 3 months (%)	1 (0.88%)	3 (5.45%)	3 (6.38%)	0.11
SF-36 Summary Scores at postoperative 3 months	Physical Component	48.59±7.65	46.11±5.22	45.72±3.13	<0.01
	Mental Component	56.65±15.62	51.02±9.37	46.85±10.94	<0.01
HSS score at postoperative 3 months		79.24±7.19	75.55±4.93	75.43±5.16	<0.01

Abbreviations: VAS, visual analogue score; ROM, range of motion; HADS, hospital anxiety and depression scale; SF-36, medical outcome study short form 36; HSS, hospital for special surgery.

postoperative 3 months (P=0.03), and higher physical component of SF-36 summary score (P=0.02), as compared with patients without SSI. However, ROM at the postoperative 3 months (P=0.16) and mental component of SF-36 summary score (P=0.86) were similar between the patients with and without SSI. Patients with SSI had a higher rate of HADS of more than 8 as compared with patients without SSI, but it did not reach significance (P=0.05).

Analysis of Preoperative Variables for Postoperative SSI

In the univariate analysis of characteristics for SSI, age (OR=1.09, 95% confident interval (CI): 1.01–1.18, P=0.03), BMI (OR=1.20, 95% CI: 1.06–1.37, P<0.01), duration of surgery (OR=1.17, 95% CI: 1.07–1.28, P<0.01), ASA (OR=8.36, 95% CI: 2.74–25.53, P<0.01), chronic lung diseases (OR=6.57, 95% CI: 1.91–22.64, P<0.01), diabetes mellitus (OR=12.53, 95% CI: 3.42–45.92, P<0.01), preoperative HADS (OR=4.67, 95% CI: 1.42–15.30, P=0.01), and passive smoking status (OR=3.66, 95% CI: 1.63–8.26, P<0.01) were significantly associated with postoperative SSI (Table 5), while other characteristics were not significant. In the multivariate analysis of characteristics for SSI, BMI (OR=1.23, 95% CI: 1.04–1.45, P=0.02), duration of surgery (OR=1.26, 95% CI: 1.08–1.47, P<0.01), ASA (OR=5.23, 95% CI: 1.43–19.12, P=0.01), and passive smoking status (OR=9.63, 95% CI: 2.47–37.49, P<0.01) maintained significance, while age, chronic lung diseases, diabetes mellitus, and preoperative HADS lost significance.

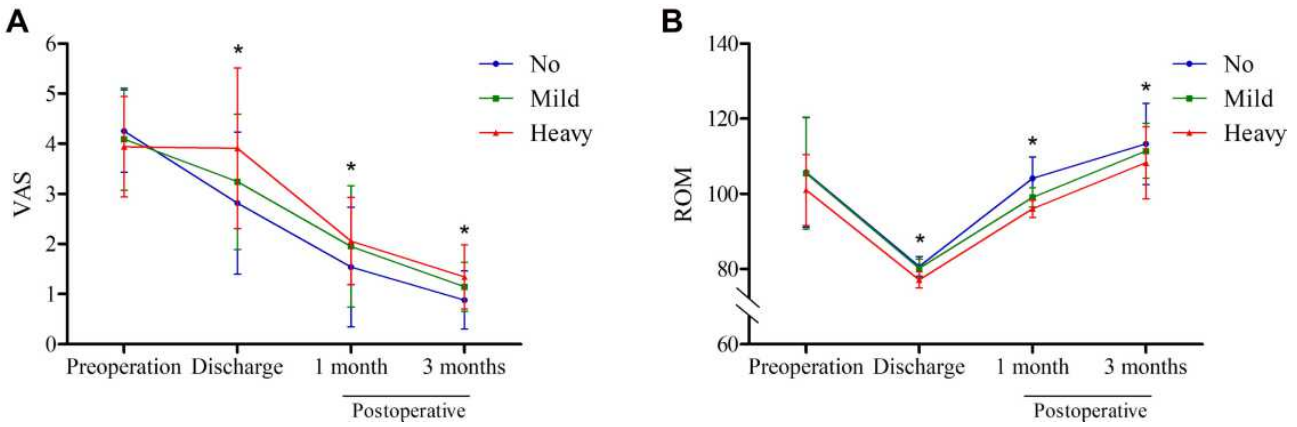

Figure 2 The visual analogue score (VAS), (**A**) and range of motion (ROM), (**B**) among the three group before, at discharge, and postoperative 1 and 3 months. *Indicating statistical significance between the three groups.

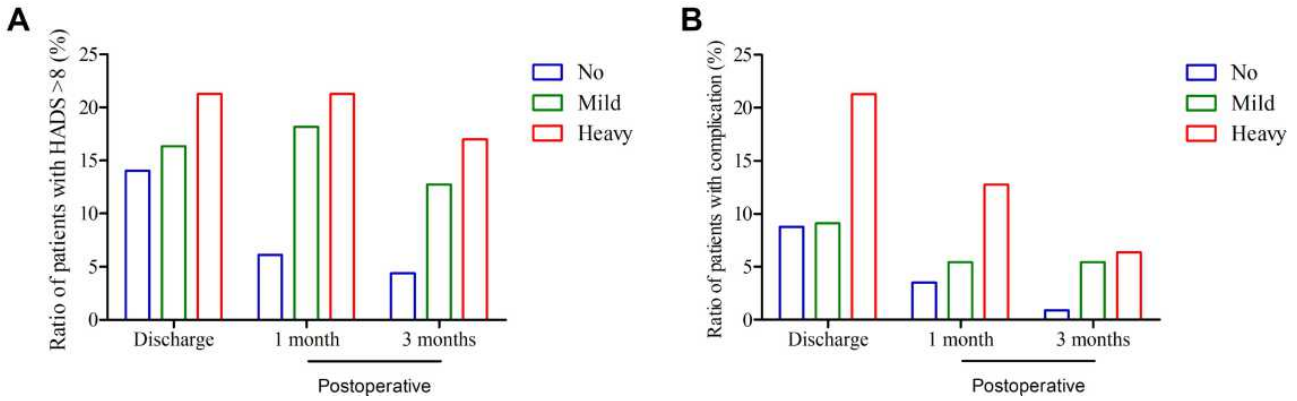

Figure 3 The anxiety and depression scale (HADS), (**A**) was significant different among the three groups at at postoperative 1 month (P=0.01) and 3 months (P=0.03). The complication rates (**B**) in the heavy smoking group was relative higher as compared with other two groups at discharge (P=0.06), postoperative 1 month (P=0.08), and 3 months (P=0.11).

The AUROC of BMI alone was 0.73, duration of surgery alone was 0.83, ASA alone was 0.76, and passive smoking status alone was 0.76. When all four significant factors were included in the model, the AUROC was up to 0.96 (Figure 4). Calibration was assessed by using the Hosmer-Lemeshow goodness-of-fit test. The test's P value was 0.96 when the model included all the four significant factors. The P-value was 0.44 for BMI alone, 0.60 for duration of surgery alone, less than 0.01 for ASA alone, and 0.56 for smoking status alone. These results indicated that except for ASA, the other three risk factors obtained good calibration ability.

Discussion

Smoking has been one of convincing and overwhelming health hazards. National data showed there were 448,865 deaths due to active cigarette smoking in 2014 in the America.[20] In 2016, the Spain scientists pointed out that one in 7 deaths in Spain could be attributable to smoking after analyzing the Spanish Health Survey and the European Health Survey.[21] Passive smoking was also proved to place negative impacts on patients undergoing surgery.[11] However, the effects of passive smoking on clinical outcomes after TKA have not been elucidated. Thus, we investigated the effects and obtained two indications. For one thing, our results indicated that passive smoking negatively affects TKA in terms of pain and functional outcomes, mental health, and the quality of life. Besides, it might also subsequently increase postoperative SSI. For another thing, passive smoking was an important independent risk factor for predicting postoperative SSI. Postoperative SSI was associated with increased hospital charges, prolonged time of hospitalization, and worse prognosis.

Table 3 Comparison of Complications Between the Three Groups at Discharge, Postoperative 1 and 3 Months

Time	Groups	Cardiovascular Diseases	Pulmonary Diseases	DVT	SSI	Neuropathies	Total (%)
Discharge	No (n=114)	4 (3.51%)	3 (2.63%)	2 (1.75%)	1 (0.88%)	0 (0.00%)	25 (55.55%)
	Mild (n=55)	2 (3.63%)	1 (1.82%)	1 (1.82%)	1 (1.82%)	0 (0.00%)	
	Heavy (n=47)	2 (4.26%)	3 (6.38%)	1 (2.12%)	4 (8.51%)*	0 (0.00%)	
Postoperative 1 month	No (n=114)	2 (1.75%)	1 (0.88%)	0 (0.00%)	1 (0.88%)	0 (0.00%)	13 (28.89%)
	Mild (n=55)	1 (1.82%)	2 (3.63%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	
	Heavy (n=47)	1 (2.12%)	2 (4.26%)	0 (0.00%)	3 (6.38%) **	0 (0.00%)	
Postoperative 3 months	No (n=114)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.88%)	7 (15.56%)
	Mild (n=55)	0 (0.00%)	1 (1.82%)	0 (0.00%)	1 (1.82%)	1 (1.82%)	
	Heavy (n=47)	0 (0.00%)	1 (2.12%)	0 (0.00%)	1 (2.12%)	1 (2.12%)	
Total number of events		12 (26.67%)	14 (31.11%)	4 (8.89%)	12 (26.67%)	3 (6.67%)	45 (100.00%)

Notes: *Indicating P=0.02, as compared between the three groups at discharge; **Indicating P=0.03, as compared between the three groups at postoperative 1 month.
Abbreviations: DVT, deep venous thrombosis; SSI, surgical site infection.

Table 4 The Comparison of Intraoperative Parameters and Postoperative Clinical Outcome Between Patients with SSI and without SSI

Variables	Patients with SSI (n=12)	Patients without SSI (n=204)	P value
Length of hospitalization (days)	18.83±0.93	12.09±4.13	<0.01
Charges in hospital	10,077.17±163.97	9765.17±346.01	<0.01
VAS at postoperative 3 months	1.42±0.51	1.02±0.60	0.03
ROM at postoperative 3 months	115.67±10.52	111.51±9.86	0.16
HADS at postoperative 3 months (>8, %)	3 (25.00%)	17 (8.33%)	0.05
SF-36 Summary Scores at postoperative 3 months			
Physical Component	51.67±10.14	47.08±6.10	0.02
Mental Component	54.67±6.09	52.99±13.76	0.86

Abbreviations: SSI, surgical site infection; VAS, visual analogue score; ROM, range of motion; HADS, hospital anxiety and depression scale; SF-36, medical outcome study short form 36.

TKA has been the main treatment for advanced arthritis and there were local and general smoking-related complications after surgery.[2,7,22] Besides, studies have shown that smoking prolonged surgical duration, added hospital charge, and increased odds of admission to intensive care unit.[23,24] A prospective study including 3908 patients

Table 5 Univariate and Multivariate Analysis of Variables for Postoperative SSI in Patients Treated with Total Knee Arthroplasty

Variables	Patients (n=216)	Simple Logistic Regression		Multiple Logistic Regression	
		OR (95% CI)	P value	OR (95% CI)	P value
Age (years)	66.05±7.80	1.09 (1.01–1.18)	0.03	Not included	
BMI (kg/m^2)	28.82±5.04	1.20 (1.06–1.37)	<0.01	1.23 (1.04–1.45)	0.02
Duration of surgery (min)	108.37±7.66	1.17 (1.07–1.28)	<0.01	1.26 (1.08–1.47)	<0.01
ASA score (%)					
1 (Healthy)	60	8.36 (2.74–25.53)	<0.01	5.23 (1.43–19.12)	0.01
2 (Minimally ill)	132				
3 (Moderately ill)	24				
Comorbidities					
Chronic heart diseases					
Yes	39	2.79 (0.79–9.83)	0.11	Not included	
No	177				
Chronic lung diseases					
Yes	25	6.57 (1.91–22.64)	<0.01	Not included	
No	191				
Diabetes mellitus					
Yes	16	12.53 (3.42–45.92)	<0.01	Not included	
No	200				
Neuropathies					
Yes	9	2.23 (0.26 −19.43)	0.47	Not included	
No	207				
Preoperative VAS	4.14±0.92	1.03 (0.55 −1.94)	0.93	Not included	
Preoperative ROM	104.64±13.80	0.99 (0.94–1.03)	0.49	Not included	
Preoperative HSS scores	56.27±16.31	1.03 (0.99–1.07)	0.18	Not included	
Preoperative HADS (>8)	42	4.67 (1.42–15.30)	0.01	Not included	
Preoperative SF-36 summary Scores					
Physical Component	33.27±4.83	0.91 (0.81–1.03)	0.15	Not included	
Mental Component	40.51±10.90	1.01 (0.96–1.07)	0.65	Not included	
Passive smoking status					
No	114	3.66 (1.63–8.26)	<0.01	9.63 (2.47–37.49)	<0.01
Mild	55				
Heavy	47				

Abbreviations: SSI, surgical site infection; BMI, body mass index; ASA, American Society of Anesthesiologists; VAS, visual analogue score; ROM, range of motion; HADS, hospital anxiety and depression scale; HSS, hospital for special surgery; SF-36, medical outcome study short form 36.

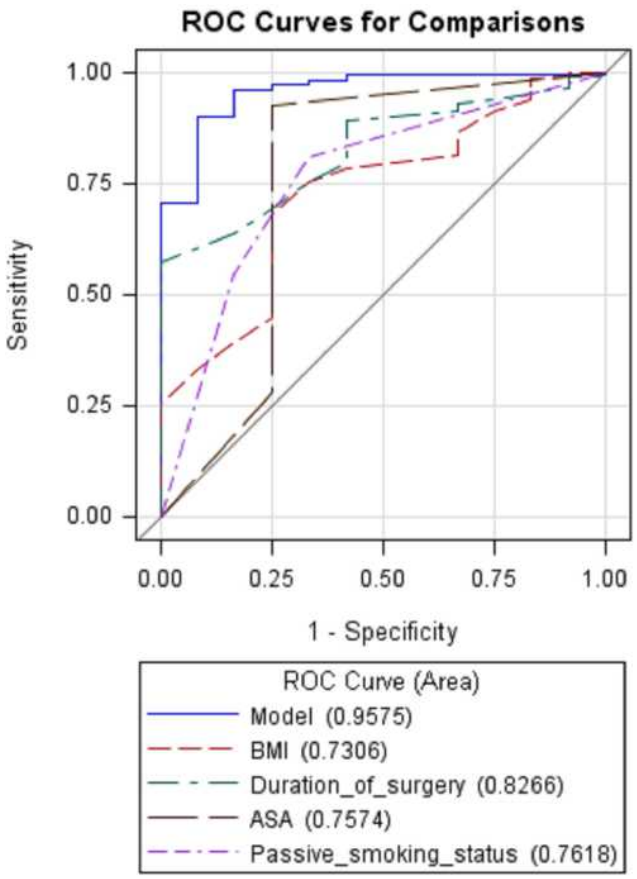

Figure 4 The area under the receiver operating characteristic curve (AUROC) for logistic model consisting of the combination of the four significant factors (AUROC=0.96), BMI alone (AUROC=0.73), duration of surgery alone (AUROC=0.83), ASA alone (AUROC=0.76), and passive smoking status alone (AUROC=0.76).

reported a significant difference between smokers and nonsmokers for SSI.[25] A research with a mean follow-up of 47 months showed that TKA in smokers had a higher increased revision rate compared with nonsmokers.[6] Perioperative smoking cessation seemed to be effective in decreasing postoperative morbidity, improving health, and saving money.[2,24,26,27] We obtained the results about what complications passive smoking might bring and the results were similar to active smoking. Nicotine, nitric oxide, and carbon monoxide may contribute to wound-related complications and injury to the vascular endothelium. More explicitly, carbon monoxide reduces the oxygen content in blood, chronic exposure to nitric oxide promotes connective tissue destruction, and nicotine acutely causes sympathetic hyperactivity.[11] Balanced neoangiogenesis is essential to repairing tissue and healing wound, and it can be negatively affected by smoking.

Furthermore, side-stream smoke may do more harm compared with mainstream smoke. More than 250 chemicals in secondhand smoke are known to be toxic and some compounds are emitted at levels up to more than 10 times greater in side-stream than in mainstream.[12] Considering that aged women were of lowered immunity and higher frequency to be exposed to passive smoking,[13] the effects of cigarette smoke on passive smokers may be more serious than on active smokers. Indeed, we observed that heavy passive smoking increased the wound-related complications during the period of hospitalization. This might explain the relationship between heavy passive smoking and the increased incisional SSI. The therapy of SSI led to extra expense and extended length of stay in the hospital, since the SSI patients needed special nursing, nutritional supplementations, and aggressive antibiotics treatments.

Postoperative pain is an important subjective characteristic to the patients and ROM of joints in the early postoperative stage is closely related to functional recovery.[28] High postoperative pain contributed to lower patient satisfaction and diminished range of motion.[29] The relationship between smoking and pain is complex and uncertain. Nicotine has analgesic properties in experimental research, whereas smoking is a risk factor for chronic pain according to clinical evidence.[30] Passive smoking affects pain in multifarious ways and pain is a comprehensive result with multiple confounders.[31] The exact reasons why patients exposed to cigarette smoke felt more pain remain elusive. Evidence showed smoking was relevant to the increased number of circulating proinflammatory cytokines and prolonged inflammation, thus increasing pain sensitivity.[32] A probable explanation in the study might be due to SSI and mental problems. SSI has related to wound-related complications which would lead to wound pain.[33] Depression and anxiety increased the postoperative pain after operation, affecting the use of pain medications.[31,34] Furthermore, smoking seemed to increase the risk of symptoms of depression and anxiety.[34,35] Patients could escape from the cigarette smoke in the hospitalization for no smoking in hospital and the stress-related to the surgery might be the main reason for depression and anxiety at baseline. However, they have to live with the active smokers and unwillingly suffer from the smoke after leaving from the hospital. Therefore, differences in depression and anxiety among these three groups were not significant in the first period but significant in another two periods. There were statistical differences concerning VAS pain scores among three groups during each period. The wound-related complications might be the main cause for

the postoperative pain and ROM during the hospitalization and the mental factors were associated with the pain and ROM after discharging from the hospital. Interestingly, the VAS value was the lowest in the heavy passive smoking group before surgery despite no significance, while heavy passive smoking patients significantly suffered more from pain after surgery. This might be because those patients had higher pain sensitivity when traumatic interventions were performed. From a patient perspective, the health-related quality of life (HRQL) was an important assessment of recovery outcomes after TKA.[36] The HRQL was associated with pain, psychological distress, and comorbidities.[37] The increasing risks of pain, anxiety, depression, and wound-related complications led to the poorer HRQL in our study. Passive smoking would be an important risk factor for lowering satisfaction in patients.

The multivariate analysis of variables for SSI showed that BMI, duration of surgery, ASA, and passive smoking status were significantly associated with postoperative SSI, which indicated that the above-mentioned four factors were independent risk factors for postoperative SSI. Evaluation of the model consisting of the four significant factors showed that the discrimination (ROC=0.96) and calibration (P=0.96) were good and that there was no evidence of a lack of fit. Previous studies have shown that BMI, duration of surgery, and ASA were important risk factors for postoperative SSI.[38,39] We found that passive smoking also played an important role in the occurrence of postoperative SSI. Thus, avoiding passive smoking might be extremely necessary for patients treated with TKA. The 5As strategy[40] and a brief Ask-Advise-Refer strategy[41] have been created as standard smoking cessation interventions, which is capable of helping patient's family members to cease smoking. Literature has reported there were two methods to evaluate the magnitude of passive smoking, and that was biomarkers of environmental tobacco, including nicotine and cotinine in blood, saliva, urine and hair,[37,42] and patient-reported questionnaire. The patients were considered as passive smokers according to the smoking habits and smokers in the family members. Although the former was relatively accurate and objective, the procedures were complex and expensive. The latter was easy to operate whereas the subjective bias would reduce the credibility of results. We recorded the time of exposure to cigarette smoke during three months after discharge to decrease the recall bias.

The limitations of this study were as follows. To begin with, we could only record the early outcomes as the time of follow-up was three months. Therefore, the long-term effect of passive smoking on TKA needs future studies. Then, it was also necessary to use a more appropriate objective method for evaluating passive smoking. The method in our study was subjective and this might contribute to measurement bias, but this method was widely used to evaluate passive smoking.[16] Lastly, professional orthopedics scores assessment, such as Knee Injury & Osteoarthritis Outcome (KOOS) and International Knee Documentation Committee (IKDC), might be capable of providing more accurate and reliable information, which were not evaluated in the study.

Conclusions

Passive smoking negatively affects TKA among female patients. It may trigger poor pain and functional outcomes, aggravate depression and anxiety, and deteriorate quality of life after discharge from hospital. Avoiding exposure to smoking environment may be beneficial among TKA female patients before and after surgery.

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Disclosure

The authors declare that they have no conflict of interest.

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