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Original Research Article

# Association of preoperative smoking with complications following major gastrointestinal surgery

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# A R T I C L E I N F O

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# ABSTRACT

*Background:* Understanding modifiable surgical risk factors is essential for preoperative optimization. We evaluated the association between smoking and complications following major gastrointestinal surgery.

*Methods:* Patients who underwent elective colorectal, pancreatic, gastric, or hepatic procedures were identified in the 2017 ACS NSQIP dataset. The primary outcome was 30-day death or serious morbidity (DSM). Secondary outcomes included pulmonary complications, wound complications, and readmission. Multivariable logistic regression was used to evaluate the association between smoking and these outcomes.

*Results:* A total of 46,921 patients were identified, of whom 7,671 (16.3%) were smokers. Smoking was associated with DSM (23.2% vs. 20.4%, OR 1.15 [1.08–1.23]), wound complications (13.0% vs. 10.4%, OR 1.24 [1.14–1.34]), pulmonary complications (4.9% vs 2.9%, OR 1.93 [1.70–2.20]), and unplanned readmission (12.6% vs. 11%, OR 1.14 [95% CI 1.06–1.23]).

*Conclusions:* Smoking is associated with complications following major gastrointestinal surgery. Patients who smoke should be counseled prior to surgery regarding risks.

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# Introduction

Postoperative complications are a significant cause of morbidity and mortality after surgery. Beyond their immediate consequences, complications may also lead to negative long-term health outcomes and are known to significantly increase healthcare costs and hospital length of stay.<sup>1–5</sup> Although some adverse outcomes following surgery are unavoidable, a significant proportion of surgical complications are thought to be preventable.<sup>6</sup> Potential targets to reduce surgical complication rates include improved patient selection, preoperative patient optimization, surgical technique, postoperative management, and institution-specific practices. One patient factor which may be a target for intervention is preoperative smoking cessation.<sup>7,8</sup>

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https://doi.org/10.1016/j.amjsurg.2021.06.002 0002-9610/© 2021 Elsevier Inc. All rights reserved. Several studies have characterized the risks of smoking among patients undergoing surgery. However, these investigations have primarily focused on specific operations, patient subpopulations, or complications which may not be readily generalizable to patients undergoing major gastrointestinal surgery.<sup>9–13</sup> Furthermore, as smoking may be particularly detrimental for patients undergoing certain types of operations, such as vascular or pulmonary procedures, the risks of smoking that are associated with these procedures may not translate to other types of surgery. Therefore, the existing literature may not adequately characterize the risk of smoking for major gastrointestinal surgery.

Major gastrointestinal operations are often performed for nonemergent indications, such as the treatment of gastrointestinal malignancies or chronic diverticulitis. Surgical intervention for these disease processes is associated with high rates of surgical complications, representing an ideal target for improvement.<sup>14</sup> As these operations are commonly performed on a non-emergent basis, preoperative optimization may improving outcomes. The objective of this study was to characterize the risk of one potentially modifiable preoperative behavior, smoking, by assessing its







association with common postoperative complications. We hypothesized that smoking is associated with death or serious morbidity, wound complications, and pulmonary complications following major elective gastrointestinal surgery.

# Materials and methods

# Data source and study population

Patients were identified in the 2017 American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP) dataset. ACS NSQIP provides a clinically abstracted national surgical dataset, the characteristics and validity of which have been previously described.<sup>15–19</sup> Patients were included in this study if they underwent major gastrointestinal surgery as identified by primary Current Procedural Terminology (CPT®) codes corresponding to major gastric, hepatic, pancreatic, or colorectal procedures (Appendix 1). Patients undergoing non-elective surgery were excluded from the study. No missing data were encountered in this dataset. Due to the use of de-identified patient data only, this study is considered non-human subjects research by the Institutional Review Board of Northwestern University.

# Predictor variables

Patients were divided into smokers and non-smokers based on a history of smoking, defined as smoking cigarettes within 12 months prior to surgery. Reported patient demographic variables included age, sex, race, and ethnicity. A composite race and ethnicity variable [non-Hispanic White, non-Hispanic Black, Hispanic, other/unknown] was created from reported race and ethnicity data. Surgical characteristics included operative time, procedure type, and wound classification. Patient clinical characteristics included body mass index (BMI), American Society of Anesthesiologists (ASA) classification, preoperative weight loss >10% of total weight, functional status, and chronic steroid use. Preoperative medical comorbidity variables included diabetes mellitus, dyspnea, severe chronic obstructive pulmonary disease (COPD), hypertension requiring medication, and disseminated cancer.

# Outcomes

The primary outcome of this study was a composite endpoint of death or serious morbidity (DSM) within 30 days of surgery. This composite variable included death, deep or organ space surgical site infection, wound dehiscence, pneumonia, ventilator dependence beyond 48 h after surgery, unplanned reintubation, deep venous thrombosis, pulmonary embolism, renal failure requiring dialysis, myocardial infarction, cardiac arrest, stroke with neurologic deficit, sepsis, septic shock, blood transfusion, or unplanned reoperation. Several versions of this outcome measure have previously been employed in studies using the ACS NSQIP dataset to evaluate severe postoperative complications and the composite measure has been endorsed by the National Quality Forum.<sup>20–22</sup> Secondary outcome measures included 30-day unplanned readmission, a composite wound complication outcome comprised of any surgical site infection or wound dehiscence within 30 days of surgery, and a composite pulmonary complication outcome comprised of pneumonia or unplanned reintubation within 30 days of surgery and prolonged ventilator dependence beyond 48 h after surgery.

# Statistical analysis

Bivariate analysis of the relationship of patient characteristics

and outcomes with smoking status was examined using chi-square tests for categorical variables, two-sample Student's t tests with equal variance for normally distributed continuous variables, and Wilcoxon rank-sum tests for non-normally distributed continuous variables. To account for confounding factors between smoking status and the study outcomes, multivariable logistic regression was utilized. Regression models were constructed incorporating characteristics that were identified as potential confounding variables based on an association with smoking status at the p < 0.05level on bivariate analysis. Preoperative dyspnea and COPD were not included in the regression models as these comorbidities are direct sequelae of smoking and therefore are hypothesized to function as an intermediate between smoking and the primary outcome. A stratified analysis was performed to evaluate whether the relationship of smoking with DSM varied based on BMI. To accomplish this, patients were divided into BMI categories (underweight, normal weight, overweight, and obese) and multivariable regression models were estimated for each category. Heteroskedasticity-robust standard errors were used for all regression models, and all significance tests were two-sided with a threshold of p < 0.05. Statistical analysis was performed using Stata version 12.1 (Statacorp LLC, College Station, TX, USA).

# Results

A total of 46,921 patients were identified who underwent colorectal (69.7%), pancreatic (16.4%), gastric (2.7%) and hepatic (11.3%) procedures. Of these, 7,671 (16.3%) were smokers and 39,250 (83.7%) were non-smokers. Patient cohorts differed in multiple demographic factors (Table 1), with smokers being younger (mean age 40.1 vs 44.6 years, p < 0.001), more likely to be classified as ASA III/IV/V than ASA I/II (64.5% vs. 59.2%, p < 0.001), and more likely to have preoperative dyspnea (8.5% vs. 5.3%, p < 0.001) and severe COPD (9.8% vs. 3.1%, p < 0.001).

Bivariate analysis (Table 2) of individual complications demonstrated increased rates among smokers of surgical site infection (12.5% vs. 10.1%, p < 0.001), including differences in superficial (4.4% vs. 3.6%, p = 0.001), deep (0.9% vs. 0.5%, p = 0.001), and organ space (8.0% vs. 6.5%, p < 0.001) infections. Increased rates of wound disruption (1.1% vs. 0.6%, p < 0.001), pneumonia (3.3% vs. 1.8%, p < 0.001), reintubation (2.1% vs. 1.3%, p < 0.001), prolonged mechanical ventilation (1.9% vs. 1.1%, p < 0.001), acute renal failure (0.6% vs. 0.4%, p = 0.016), sepsis (4.2% vs. 3.6%, p = 0.008), septic shock (1.8% vs. 1.2%, p < 0.001), and unplanned reoperation (5.7% vs. 4.2%, p < 0.001) were also seen for smokers compared to nonsmokers. Mean length of stay was increased for smokers compared to non-smokers (6.8 [SD 6.5] vs. 6.3 [SD 6.1] days, p < 0.001).

After adjusting for patient comorbidities and operative procedure (Table 3), patients who smoked had an increased likelihood of DSM compared to non-smokers (23.2% vs. 20.4%, OR 1.15, 95% CI 1.08-1.23, p < 0.001). Smokers also had increased likelihood of wound complications (13.0% vs. 10.4%, OR 1.24, 95% CI 1.14-1.34, p < 0.001) and pulmonary complications (4.9% vs. 2.9%, OR 1.93, 95% CI 1.70–2.20, *p* < 0.001). Odds of unplanned readmission were also higher in smokers (12.6% vs. 11.0%, OR 1.14, 95% CI 1.06-1.23, p = 0.001). On stratified analyses, there was no association between smoking and DSM among underwent patients (28.6% vs. 27.7%, OR 0.91, 95% CI 0.67–1.26, *p* = 0.58; Table 4). However, smoking was associated with DSM among patients with normal BMI (24.2% vs. 20.5%, OR 1.13, 95% CI 1.02–1.26, p = 0.02), patients who were overweight (22.0% vs. 20.3%, OR 1.13, 95% CI 1.01–1.27, *p* = 0.04) and patients who were obese (22.3% vs. 20.1%, OR 1.21, 95% CI 1.08-1.36, p = 0.001).

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#### Table 1

Patient and procedure characteristics by smoking status.

	$\frac{\text{Smoker}}{\text{N} = 7671}$	$\frac{\text{Non-smoker}}{\text{N} = 39,250}$	P value
Mean age, years (SD)	40.1 (12.3)	44.6 (14.8)	<0.001
Sex, n (%)			< 0.001
Male	4,082 (53.2)	18,906 (48.2)	
Female	3,589 (46.8)	20,344 (51.8)	
Race/ethnicity, n (%)			< 0.001
Non-Hispanic White	5,209 (67.9)	26,907 (68.6)	
Non-Hispanic Black	817 (10.7)	2,964 (7.6)	
Hispanic	580 (7.6)	3,869 (9.9)	
Other	1,065 (13.9)	5,510 (14.0)	
BMI in kg/m <sup>2</sup> , mean (SD)	27.6 (6.5)	28.7 (6.4)	< 0.001
ASA class, n (%)			< 0.001
I/II	2,721 (35.5)	16,015 (40.8)	
III/IV/V	4,943 (64.5)	23,205 (59.2)	
Functional status, n (%)			0.128
Independent	7,548 (98.4)	38,521 (98.1)	
Dependent	123 (1.6)	729 (1.9)	
Operative time in minutes, mean (SD)	233.6 (123.5)	229.6 (124.7)	0.009
Procedure type, n (%)			0.019
Colorectal	5,286 (68.9)	27,403 (69.8)	
Pancreatic	1,330 (17.3)	6,364 (16.2)	
Gastric	225 (2.9)	1,023 (2.6)	
Liver	830 (10.8)	4,460 (11.4)	
Wound class, n (%)			< 0.00
Clean	300 (3.9)	1,570 (4.0)	
Clean-contaminated	5,840 (76.1)	31,275 (79.7)	
Contaminated	1,004 (13.1)	4,530 (11.5)	
Dirty	527 (6.9)	1,875 (4.8)	
Weight loss $>10\%$ in last 6 months, n (%)	507 (6.6)	1,748 (4.5)	< 0.00
Preoperative comorbidities, n (%)		,	
Diabetes mellitus	1,181 (15.4)	7,036 (17.9)	< 0.00
Dyspnea	655 (8.5)	2,091 (5.3)	< 0.001
Severe COPD	754 (9.8)	1,219 (3.1)	<0.001
Hypertension requiring medication	3,256 (42.5)	18,743 (47.8)	< 0.00
Steroid use for chronic condition	405 (5.3)	2,804 (7.1)	< 0.00
Disseminated cancer	694 (9.1)	3,931 (10.0)	0.009
Pre-existing open or infected wound	99 (1.3)	383 (1.0)	0.012

Abbreviations: SD, standard deviation; BMI, body mass index; ASA, American Society of Anesthesiologists; COPD, chronic obstructive pulmonary disease.

#### Table 2

Incidence of individual complications by smoking status.

	Smoker N = 7671	Non-smoker N = 39,250	P value
30-day mortality, n (%)	96 (1.3)	416 (1.1)	0.140
Any surgical site infection, n (%)	956 (12.5)	3,975 (10.1)	< 0.001
Superficial	338 (4.4)	1,427 (3.6)	0.001
Deep	69 (0.9)	223 (0.5)	0.001
Organ space	611 (8.0)	2,532 (6.5)	< 0.001
Wound disruption, n (%)	84 (1.1)	248 (0.6)	< 0.001
Pneumonia, n (%)	2499 (3.3)	709 (1.8)	< 0.001
Unplanned reintubation, n (%)	162 (2.1)	504 (1.3)	< 0.001
Ventilator >48 h, n (%)	142 (1.9)	428 (1.1)	< 0.001
DVT/thrombophlebitis, n (%)	104 (1.4)	533 (1.4)	0.988
Pulmonary embolism, n (%)	58 (0.8)	273 (0.7)	0.562
Progressive renal insufficiency, n (%)	65 (0.9)	275 (0.7)	0.166
Acute renal failure, n (%)	46 (0.6)	158 (0.4)	0.016
Urinary tract infection, n (%)	148 (1.9)	898 (2.3)	0.052
Stroke with neurologic deficit, n (%)	23 (0.3)	74 (0.2)	0.050
Myocardial infarction, n (%)	59 (0.8)	259 (0.7)	0.286
Cardiac arrest requiring CPR, n (%)	43 (0.6)	191 (0.5)	0.401
Blood transfusion, n (%)	672 (8.8)	3,762 (9.6)	0.024
C. diff colitis, n (%)	77 (1.0)	437 (1.1)	0.399
Sepsis, n (%)	324 (4.2)	1,414 (3.6)	0.008
Septic shock, n (%)	135 (1.8)	483 (1.2)	< 0.001
Unplanned reoperation, n (%)	440 (5.7)	1,641 (4.2)	< 0.001
Length of stay in days, mean (SD)	6.8 (6.5)	6.3 (6.1)	< 0.001

Abbreviations: DVT, deep vein thrombosis; CPR, cardiopulmonary resuscitation; SD, standard deviation.

#### Discussion

Complications following major gastrointestinal operations significantly contribute to the morbidity and mortality associated with these procedures. Previous studies have demonstrated the deleterious effect of smoking on outcomes following many types of surgical procedures.<sup>9–13</sup> This study expands on the existing literature by quantifying the association of smoking with complications after elective major abdominal and pelvic surgery. Our results demonstrate an association between smoking and a number of complications. Overall odds of DSM following major abdominal and pelvic surgery are substantially increased in patients who smoke, suggesting that smokers are at increased risk of serious surgical complications. The association of smoking with DSM is particularly strong among patients with elevated BMI. These finding agrees with the existing literature. Increased odds of DSM among smokers have been demonstrated in prior studies of patients who undergo elective hernia repair (30%),<sup>23</sup> bariatric surgery (13%),<sup>20</sup> and thoracic procedures (44%).<sup>9</sup>

There are several possible explanations for this finding. First, active smoking is known to have direct deleterious effects on the pulmonary, cardiovascular, and immune systems. Smoking has been shown to impair the clearance of, and immune response to, respiratory bacterial pathogens resulting in an increased risk of pneumonia.<sup>24</sup> Additionally, smoking affects wound healing by decreasing local tissue oxygenation, impairing the inflammatory

#### Table 3

Association of complications with smoking.

	Smokers	Non-smokers	OR (95% CI) <sup>a</sup>	P value
	N = 7671	N = 39,250	N = 39,250	
Death or serious morbidity	1,776 (23.2)	8,023 (20.4)	1.15 (1.08–1.23)	<0.001
Wound complication	994 (13.0)	4,091 (10.4)	1.24 (1.14-1.34)	< 0.001
Pulmonary complication	375 (4.9)	1,141 (2.9)	1.93 (1.70-2.20)	< 0.001
Unplanned readmission	969 (12.6)	4,307 (11.0)	1.14 (1.06–1.23)	0.001

Abbreviations: OR, odds ratio; CI, confidence interval.

<sup>a</sup> Adjusted odds ratios for each complication for smokers compared to non-smokers including age, sex, race/ethnicity, body mass index, American Society of Anesthesiologists class, procedure type, functional independence status, operative time, wound class, weight loss >10% of total body weight, diabetes mellitus, hypertension, steroid use, disseminated cancer, and pre-existing open or infected wound as covariates.

#### Table 4

Association of smoking with death and serious morbidity, stratified by BMI.

	Total, n (%)	Death or Serious Morbidity, n (%)	OR (95% CI) <sup>a</sup>	P value
Underweight (BMI <18.5	kg/m <sup>2</sup> )			
Smoker	336 (31.8)	96 (28.6)	0.91 (0.67-1.26)	0.58
Non-smoker	722 (68.2)	200 (27.7)	1 (REF)	_
Normal weight (BMI 18.5	$-25 \text{ kg/m}^2$			
Smoker	2686 (19.3)	650 (24.2)	1.13 (1.02-1.26)	0.02
Non-smoker	11,254 (80.7)	2304 (20.5)	1 (REF)	-
Overweight (BMI 25-30	kg/m <sup>2</sup> )			
Smoker	2332 (15.0)	513 (22.0)	1.13 (1.01-1.27)	0.04
Non-smoker	13,241 (85.0)	2689 (20.3)	1 (REF)	-
Obese (BMI $\geq$ 30 kg/m <sup>2</sup> )				
Smoker	2292 (14.2)	511 (22.3)	1.21 (1.08-1.36)	0.001
Non-smoker	13,841 (85.8)	2786 (20.1)	1 (REF)	_

Abbreviations: OR, odds ratio; CI, confidence interval; BMI, body mass index.

<sup>a</sup> Analysis of the association of death and serious morbidity for smokers compared to non-smokers, stratified by BMI category. Multivariable logistic regression models included age, sex, race/ethnicity, American Society of Anesthesiologists class, procedure type, functional independence status, operative time, wound class, weight loss >10% of total body weight, diabetes mellitus, hypertension, steroid use, disseminated cancer, and pre-existing open or infected wound as covariates.

response, and downregulating proteolytic and synthetic enzyme activity.<sup>25</sup> A second possibility is that smoking indirectly increases the risk of complications through its known association with comorbidities including heart disease, hypertension, or COPD. Finally, it is possible that smoking may simply be a marker of poor health status. Our study most strongly supports a direct and indirect causative mechanism. In our study, wound complications are responsible for substantial proportion of the overall DSM and the odds ratios for these complications among smokers are especially high. Given the well-defined short-term impairments in wound healing associated with active smoking, this finding is likely explained primarily by a direct toxic effect of smoking on the wound healing process. An indirect causative role is also likely important, as smoking is known to cause chronic damage to the lung parenchyma, resulting in reduced lung function.<sup>26</sup> This mechanism likely plays a role, along with the direct short-term effects of tobacco smoking, in the significantly increased odds of pulmonary complications noted among smokers. Although the ability to adjust for confounders is incomplete due to undiagnosed or unmeasured comorbidities, we incorporated multiple markers of health, such as age, BMI, and ASA class into our models as covariates to minimize their impact. Additionally, other unmeasured factors, such as surgeon characteristics or technique, may influence postoperative outcomes. However, these characteristics would not be expected to differ significantly based on a patient's smoking status and are therefore are unlikely to negatively impact this analysis.

The results of this study provide important insight that may help guide efforts to reduce surgical complications after major elective gastrointestinal surgery. Smoking is a modifiable risk factor, as studies have shown that even short-term smoking cessation for several weeks results in reversal of the pathophysiologic effects of smoking.<sup>25</sup> In many cases, major abdominal and pelvic surgeries are performed for indications that, although time sensitive, are not emergent, including malignancy, chronic diverticulitis, or other benign indication. Therefore, ample opportunity likely exists for behavior change prior to surgery. As complications can have substantial effects beyond the immediate postoperative period, the potential benefit of preventing complications is substantial.<sup>27–30</sup> Therefore, any opportunity to reduce the risk of complications through modification of patient behavior or preparation prior to surgery is an important target for quality improvement.

In recent years, increasing attention has been given to preoperative optimization and "prehabilitation".<sup>31</sup> A number of clinical trials have evaluated the effectiveness of preoperative smoking cessation programs. These include studies of patients undergoing vascular,<sup>32</sup> cardiac,<sup>33</sup> orthopedic,<sup>34</sup> breast,<sup>35</sup> hernia repair,<sup>36</sup> or other elective operations<sup>37–39</sup> and employ a variety of smoking cessation techniques. In these studies, smoking cessation programs varied in their effectiveness to achieve abstinence or reduce operative complications. However, a meta-analysis demonstrated reduced risk of wound complications for patients who received a smoking cessation intervention.<sup>25</sup> Smoking is not the only risk factor for postoperative complications, and many other patient characteristics, disease factors, and surgeon characteristics contribute to postoperative outcomes. Our work provides additional evidence that smoking in the preoperative period is one potentially risk factor for surgical complications and that interventions targeting preoperative smoking cessation, especially among obese patients, may be an important part of pre-surgical optimization and avoidance of preventable complications.

This study has several limitations that should be considered when interpreting the data presented. First, as a retrospective study, only association, and not causation, between smoking and the examined outcomes can be definitively concluded. Despite this limitation, the strong body of evidence linking smoking with similar sequelae and the well-described mechanisms by which B.C. Brajcich, T.K. Yuce, R.P. Merkow et al.

smoking negatively impacts different organ systems strengthen the argument that smoking increases the risk of complications, both directly and indirectly. Second, the dataset utilized for this work does not quantify the exposure to smoking, but rather simply assesses whether the patient smoked in the year leading up to surgery. This results in an inability to assess a dose-dependent relationship between smoking and complications. Additionally, this limits the ability of the study to measure the chronic effects of a smoking in individuals who quit more than one year prior to surgery. Despite this limitation, measuring the short-term effects of smoking provides a risk-assessment profile more germane for behavior modification interventions in the pre-surgical setting. Finally, the ACS NSQIP dataset does not include additional variables, such as surgeon experience or technical skill, which contribute to postoperative outcomes. Although these factors are known to be important determinants of postoperative outcomes, it is unlikely that they differ substantially between smokers and non-smokers. Therefore, although they may play an independent role in postoperative outcomes, it is unlikely that their omission introduces substantial bias into the association of smoking with postoperative complications assessed in this study.

### Conclusion

Smoking status is associated with increased odds of death and serious morbidity following major gastrointestinal surgery. Furthermore, wound and pulmonary complications are particularly elevated in smokers compared with non-smokers. This study strengthens the argument that smoking may contribute to postoperative morbidity and that smoking cessation is an important target for prevention of postoperative complications. Therefore, patients who smoke should be counseled about the potentially increased risks of complications prior to elective gastrointestinal surgery. Surgeons should understand the importance of preoperative smoking cessation and actively incorporate assessment of smoking status and pathways for smoking cessation counselling into the preoperative evaluation of patients undergoing gastrointestinal surgery.

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# **Declaration of competing interest**

The authors declare that they have no conflicting interests, financial or otherwise, related to this work.

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#### Appendix 1. Current Procedural Terminology (CPT) Codes

Gastric43611, 43620, 43621, 43622, 43631, 43632, 43633, 43634Hepatic47120, 47122, 47125, 47130

- Pancreatic 48120, 48140, 48145, 48146, 48148, 48150, 48152, 48153, 48154, 48155
- Colorectal 44140, 44141, 44143, 44144, 44145,44146, 44147, 44150, 44151, 44160, 44204, 44205, 44206, 44207, 44208, 44210, 44155, 44156, 44157, 44158, 44211, 44212, 45110, 45111, 45112, 45113, 45114, 45116, 45119, 45120, 45121, 45123, 45126, 45130, 45135, 45160, 45395, 45397, 45402, 45550

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