# Effects of red yeast rice prescription (LipoCol Fort) on adverse outcomes of surgery

Ta-Liang Chen[1,2,3], Chun-Chieh Yeh[4,5], Chao-Shun Lin[1,2,3], Chun-Chuan Shih[6,7], Chien-Chang Liao[1,2,3,8,9]

[1]Department of Anesthesiology, Taipei Medical University Hospital, Taipei, Taiwan
[2]Health Policy Research Center, Taipei Medical University Hospital, Taipei, Taiwan
[3]Department of Anesthesiology, School of Medicine, College of Medicine, Taipei Medical University, Taipei, Taiwan
[4]Department of Surgery, China Medical University Hospital, Taichung, Taiwan
[5]Department of Surgery, University of Illinois, Chicago, United States of America
[6]School of Chinese Medicine for Post-Baccalaureate, College of Medicine, I-Shou University, Kaohsiung, Taiwan
[7]Ph.D. Program for the Clinical Drug Discovery from Botanical Herbs, Taipei Medical University, Taiwan
[8]School of Chinese Medicine, China Medical University, Taichung, Taiwan
[9]Department of Anesthesiology, Shuang Ho Hospital, Taipei Medical University, New Taipei City, Taiwan
*Corresponding author:
Chien-Chang Liao, PhD, MPH
Associate professor
Department of Anesthesiology
Taipei Medical University Hospital
252 Wu-Xing Street, Taipei 110, Taiwan
Tel: +886-2-27372181 ext.8310; Fax: +886-2-27367344
E-mail: jacky48863027@yahoo.com.tw; ccliao@tmu.edu.tw

Abstract: 243; Text: 2248; Tables: 3; Figure: 0 ; Supplementary file : 0
Key Words: red yeast rice; surgery; adverse outcome
Running header: Red Yeast Rice on surgical outcomes

List of abbreviations: CI=confidence interval; ICD-9-CM=International Classification of Diseases, Ninth Revision, Clinical Modification; RYR=Red Yeast Rice; OR, Odds Ratio.

**Funding:** Taiwan's Ministry of Science and Technology (MOST107-2221-E-038-009; MOST106-2314-B-038-036-MY3; MOST106-2221-E-038-003; MOST106-2320-B-214-003).

**Competing interests:** None reported.

**Authors' contributions:** CCL: conception and design, analysis and interpretation of the data, drafting the article, critical revision of the manuscript for important intellectual content and final approval of the version to be published. TLC, CCY, CSL, CCS: conception and design, interpretation of the data, critical revision of the manuscript for important intellectual content

and final approval of the version to be published. Prof. Chun-Chuan Shih has equal contribution with first author.

**Acknowledgements:** This study is based in part on data obtained from the National Health Insurance Research Database. This database is provided by the Bureau of National Health Insurance of Taiwan's Ministry of Health and Welfare, and is managed by the National Health Research Institutes. The authors' interpretations and conclusions do not represent those of the Bureau of National Health Insurance, the Ministry of Health and Welfare, or the National Health Research Institutes.



## ABSTRACT

**Background:** The influence of red yeast rice (RYR) on perioperative outcome remains unknown.

**Aim:** We aimed to compare the complications and mortality after surgery between patients treated with and without RYR prescription.

**Design:** In this surgical cohort study of 3.6 million surgical patients who underwent major inpatient surgeries, 2581 patients who used RYR prescription preoperatively were compared with 25,810 non-RYR patients selected by matching for age and sex.

**Methods:** Patients' demographics and medical conditions were collected from the claims data of the National Health Insurance in Taiwan. Complications and mortality after major surgeries in association with RYR prescription were investigated by calculating adjusted odds ratios (ORs) and 95% confidence intervals (CIs) by multiple logistic regression.

**Results:** Compared with patients without RYR prescription, patients prescribed RYR had

lower risks of postoperative bleeding (OR 0.36, 95% CI 0.15-0.89), pneumonia (OR 0.54, 95% CI 0.36-0.83), stroke (OR 0.66, 95% CI 0.47-0.92), and 30-day in-hospital mortality (OR 0.37, 95% CI 0.15-0.92). Decreased risk of intensive care (OR 0.64, 95% CI 0.54-0.77), shorter length of hospital stay ($p < 0.001$), and lower medical expenditures ($p = 0.0008$) during the index surgical admission were also noted for patients with RYR prescription compared to those for patients without RYR prescription.

**Conclusions:** This study showed a potentially positive effect of RYR on outcomes after major surgeries. However, patient noncompliance for taking medication should be noted. Our findings require future prospective studies to validate RYR prescription for improving perioperative outcomes.

## Introduction

Traditional Chinese medicine (TCM) has been commonly used in Asian populations.[1] TCM has also been considered complementary and alternative medicine, with an increasing trend of utilization in Western countries.[2,3] Although the therapeutic effects of TCM have been investigated among patients with various diseases, such as stroke, cancer, pain, and allergic rhinitis, in several well-designed studies,[4] limited information is available about whether TCM is helpful in improving outcomes in patients undergoing surgery.

Red yeast rice (RYR) also called *Monascus purpureus* Went rice, is an herbal medicine that has been frequently prescribed by physicians at TCM clinics. Despite its limitations, the effects of RYR have been proven to reduce total cholesterol, low-density lipoprotein cholesterol, triglycerides, and lipid ratios in patients with hyperlipidemia.[5-12] Even among patients using antipsychotics, a daily dose of at least 200 mg of RYR for 30 days was suggested to be effective for preventing and/or treating hyperlipidemia.[13] The anti-inflammatory effect of RYR was also found to be helpful in reducing cardiovascular diseases.[10,11] In addition, some studies suggested that people who used RYR had decreased risk of cancer compared with that in patients who did not use RYR.[14] There is growing evidence suggesting that aside from improving lipid profiles, RYR could also be used to improve general health.

Among 66 countries reporting surgical data, it was estimated that 312.9 million operations

took place in 2012, representing a 33.6% increase over 8 years.[15] A high prevalence of dyslipidemia was also investigated in the Chinese population, and the use of RYR was common in the Chinese population.[16] However, the effects of RYR on perioperative outcomes in surgical patients remain unknown. Using claims data from the insurance program in Taiwan, we conducted a population-based study to compare the risk of complications and mortality after major surgeries in patients with and without the use of RYR prescription.

## Materials and methods

### Source of data

Taiwan's Health Insurance Program was implemented in 1995 and now covers more than 99% of the 23 million residents with comprehensive health services. Details of the database for the insurance program and related available information have been described in our previous studies.[4,17,18] To protect personal privacy, the electronic database was decoded and patient identifications were scrambled for further public access for research. According to the corresponding regulations, informed consent is not required because of the use of decoded and scrambled patient identification. Our study was also evaluated and approved by the joint institutional review boards of Taipei Medical University (TMU-JIRB-201710033).

### Study design

Among 3.6 million surgical patients who underwent major inpatient surgeries in Taiwan in 2008-2013, we examined medical claims and identified 2581 people aged ≥20 years who had received a physician's prescription for RYR within 24 months prior to the index surgery. Each patient who underwent surgery and received RYR prescription was randomly matched to a surgical patient who did not use RYR, using a propensity score matched-pair procedure (case-control ratio, 1:1) to adjust for sociodemographics, medical conditions, previous medial visits, types of surgery and types of anesthesia.

### Definition and criteria

For appropriately identifying RYR users in this study, we defined people who visited TCM clinics and received physician's prescription for RYR under the coverage of Taiwan's Health Insurance Program. In this study, an RYR prescription is concentrated Chinese herbal medicine, LipoCol Forte®. Different from biochemical medications, LipoCol Forte is a natural herbal medicine, and each capsule of LipoCol Forte contains 600 mg *Monascus purpureus* Went rice including the index component lovastatin 5.7 mg. Under a physician's standard directions, patients with hyperlipidemia (total cholesterol ≥200 mg/dL and/or low-density lipoprotein cholesterol ≥ 130 mg/dL and/or triglyceride ≥ 200 mg/dL) take 2 capsules per day for at least one month. In this study, we defined major inpatient surgeries as procedures requiring general, epidural, or spinal anesthesia and the index surgery with hospitalization for >1 day. Low-income status was defined as having a low income within 2 years before surgery, and this definition (waiving copayment when receiving medical care) was verified by the Ministry of Health and Welfare.

The International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) administration codes and physicians' diagnoses were used to identify the history of disease (within preoperative 24 months) and postoperative complications (that occurred during the index admission) for surgical patients.[4,17,18] These medical conditions and postoperative complications were determined from medical claims for the 24-month preoperative period and included hypertension, mental disorders, diabetes, ischemic heart

disease, chronic obstructive pulmonary diseases, liver cirrhosis, heart failure, renal dialysis, postoperative bleeding, pneumonia, septicemia, urinary tract infection, deep wound infection, stroke, acute myocardial infarction, acute renal failure, and pulmonary embolism. A requirement for intensive care, the length of hospital stay, and medical expenditures during the index surgical admission were also compared between patients with and those without preoperative RYR prescription.

**Statistical analysis**

We used a propensity score-matched pair analysis to determine associations between RYR prescription and postoperative outcomes. A nonparsimonious multivariable logistic regression model was used to estimate a propensity score for surgical patients receiving RYR. The targeted covariates for balance between surgical patients with and without RYR prescription included age, sex, low income, hypertension, mental disorders, diabetes, ischemic heart disease, chronic obstructive pulmonary diseases, liver cirrhosis, heart failure, renal dialysis, history of emergency care, history of inpatient care, types of surgery and anesthesia.

Categorical variables are summarized using frequencies (percentages) and were compared between people who used RYR prescription and those who did not by using chi-square tests. Continuous variables are summarized using means ± standard deviations and were compared using t-tests. Adjusted odds ratios (ORs) and 95% confidence intervals (CIs) of postoperative complications and mortality associated with RYR prescription were calculated by multiple

logistic regression. Additional analyses stratified by age, sex, number of medical conditions, emergency care and inpatient care were also performed for examining surgical outcomes among RYR prescription recipients within these strata.

## Results

Under the propensity-score matching procedure, Table 1 shows the balance in age and sex between surgical patients with and without RYR prescription. Higher proportions of neurosurgery, general anesthesia, hypertension, mental disorders, diabetes, ischemic heart disease, chronic obstructive pulmonary diseases, liver cirrhosis, and renal dialysis were found in patients with RYR prescription than those found in controls (all at significant differences of $p<0.05$).

After adjustment in multiple logistic regressions (Table 2), patients with RYR prescription had lower risks of postoperative bleeding (OR 0.36, 95% CI 0.15-0.89), pneumonia (OR 0.54, 95% CI 0.36-0.83), stroke (OR 0.66, 95% CI 0.47-0.92), and 30-day mortality (OR 0.37, 95% CI 0.15-0.92) than did the control group. Using RYR prescription was associated with decreased risk of intensive care after surgery (OR 0.64, 95% CI 0.54-0.77). Shorter length of hospital stay (6.1±7.1 vs. 7.6±9.7 days, $p<0.0001$) and lower medical expenditures (2480±3271 vs. 2709±3795 US dollars, $p=0.0008$) were also noted for patients with RYR prescription than for those without RYR prescription.

In the stratified analysis (Table 3), reduced risk of postoperative adverse events (including postoperative bleeding, pneumonia, stroke, intensive care, and mortality) was associated with RYR prescription in subgroups of females (OR 0.57, 95% CI 0.44-0.72), males (OR 0.69, 95% CI 0.55-0.86), and patients aged ≥50 years. The association between RYR prescription

and reduced risk of postoperative adverse events was significant in patients with no hospitalization (OR 0.63, 95% CI 0.52-0.78), ≥2 hospitalizations (OR 0.44, 95% CI 0.28-0.67), no emergency visit (OR 0.68, 95% CI 0.55-0.84), one emergency visit (OR 0.60, 95% CI 0.43-0.85), ≥2 emergency visits (OR 0.55, 95% CI 0.38-0.79), one medical condition (OR 0.56, 95% CI 0.43-0.74), and ≥2 medical conditions (OR 0.53, 95% CI 0.39-0.70).

The adjusted ORs of postoperative adverse events for patients with 1-90, 91-180, ≥181 cumulative consumption of RYR capsules were 0.70 (95% CI 0.57-0.85), 0.63 (95% CI 0.41-0.97), and 0.65 (95% CI 0.47-0.91), respectively, compared with people without RYR prescriptions (Table 4)

## Discussion

In this population-based study with multiple regression adjustment, we found that patients who used RYR prescription had decreased postoperative complications, intensive care use, mortality, length of hospital stay, and medical expenditures compared with patients with no use of RYR prescription. The significant association between reduced risk of postoperative adverse events and RYR prescription could be observed in several subgroups.

For eliminating the confounding bias from age and sex, we used frequency matching by age and sex for investigating perioperative outcomes between patients with and without use of RYR prescription. Information from previous reports suggested that economic status, history of diseases, coexisting medical conditions, types of surgery, and types of anesthesia were factors associated with perioperative outcomes.[17,18] People with hypertension, diabetes, and heart diseases were common potential users of lipid-lowering agents.[19,20-22] For calculating appropriate risk of postoperative complications and mortality in patients with RYR prescription, we applied multiple logistic regression to control the above potential confounding factors.

Regarding the beneficial effects of RYR prescription on perioperative outcomes, we proposed some possible explanations. First, it was confirmed that RYR reduces total cholesterol, low-density lipoprotein cholesterol, triglyceride, and lipid ratios for patients with hyperlipidemia.[5-12] Because hyperlipidemia is an important risk factor for stroke, the

preventive effect of RYR for stroke is also reasonable, and this evidence explains why we observed a reduced risk of postoperative stroke in patients who used RYR prescription. Second, RYR contains a component (monacolin K) of lovastatin that inhibits β-hydroxy-β-methylglutaryl-CoA reductase.[23] Experimental and clinical studies suggest that statins exhibit anti-inflammatory activity that reduces the risk of pneumonia and related outcomes.[24-26] This activity may help us to explain why patients with RYR prescription had a significant reduction in postoperative pneumonia risk in this study. Third, RYR extract inhibits high-glucose-induced β-galactosidase activation and reduces high-glucose-induced oxidative stress in proangiogenic cells in a dose-dependent manner.[27] RYR-olive extract supplement also significantly reduces lipoprotein-associated phospholipase A2 in correlation with the marked reduction in plasma oxidized low-density lipoprotein cholesterol, which may lead to a reduced risk for cardiovascular disease.[28] The antioxidative effect of RYR also helps us to explain the reduced complications and mortality after surgery in patients who used RYR prescription in this study.

In the clinical setting, TCM physicians always admonish their patients not to use statin drugs during the treatment course of RYR prescription. Adherence to statin therapy is challenging in clinical practice due to statin-associated muscle symptoms.[20-22] However, we found that very few (3.5%) patients used statins during the course of RYR treatment in this study. The reduced risk of postoperative adverse events associated with RYR prescription

remains significant after excluding patients with the use of statins. Because the association between RYR prescription and reduced risk of postoperative adverse events was not significant in some subgroups, we suggest future clinical trials to solve this problem.

The complex of secondary metabolites of RYR increases the difficulty for researchers to understand its mechanism action.[29] Because RYR preparations have considerable variability in monacolin K content, predicting or understanding dose-related efficacy and side-effect risks of RYR is not easy.[30] A previous study also found striking variability in monacolin content in 12 proprietary RYR products.[31] A review article clearly recommended against red yeast rice sales or consumption until the Food and Drug Administration was ready to inspect the content and purity of all RYR preparations marketed and to provide strict current good manufacturing practice quality controls, regulations, and standards of extractions and ingredients.[30] Although RYR may have potential as an alternative lipid-lowering agent, the need for improving quality control, standardization, and exact labeling of RYR products has been highly suggested.[31] Until this occurs, physicians should be cautious in recommending RYR to their patients for the treatment of hyperlipidemia and primary and secondary prevention of cardiovascular disease.[31] Under the cumulative evidence in the available literature, the unpredictable strength and composition of RYR supplements sold at mainstream retail stores suggests that more regulations are necessary.[32]

Intake of RYR decreases levels of total cholesterol, low-density lipoprotein cholesterol, and

triglycerides and may be a treatment option for dyslipidemic patients who cannot tolerate statin therapy.[12,20-22] However, the side effects and adverse events after using RYR should be cautioned critically. A study found the presence of citrinin in one-third of the formulations tested in 12 proprietary RYR products.[31] A recent study suggested the importance of exploring multiple databases in the safety assessment of RYR products, which should be monitored by clinicians for muscular and hepatic safety, and called for urgent review by policymakers to standardize their regulatory status.[33] Only when the mild profile of adverse reactions can be confirmed in studies with adequate methodology for safety assessment might RYR be a safe and effective treatment option for dyslipidemia and cardiovascular risk reduction in statin intolerant patients.[11,20-22]

Some study limitations must be noted when interpreting our findings. First, the insurance database lacked detailed information on sociodemographic and lifestyle factors, such as education, occupation, smoking, alcohol consumption, and physical activity. Therefore, we could not evaluate their impacts on perioperative outcomes in this study. Second, some physicians may prescribe RYR with additional out-of-pocket money that was not covered in the public insurance payment. Therefore, some patients in the control group may have used noninsurance-covered RYR prescriptions, and this misclassification may lead to underestimation of the therapeutic effects of RYR prescription in the treatment group. That is, this discrepancy would likely have biased the study results toward the null hypothesis if such

misclassifications occurred. Third, residual confounding in this study remains possible, although we used frequency matching and confounding adjustment in the multiple logistic regression. In addition, we have to emphasize that a physician's prescription is not equal to a patient's intake because patient noncompliance commonly occurs in nonclinical settings. Finally, our study was an observational study that could not provide causal inference for the association between RYR prescription and reduced risk of postoperative adverse events.

In conclusion, we found that patients who underwent surgery and received RYR prescription were protected from postoperative bleeding, pneumonia, stroke and in-hospital mortality after major surgery compared with patients who did not receive RYR prescription before surgery. However, the actual biochemical mechanism underlying RYR prescription requires future prospective studies to provide solid evidence.

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and CAERS reporting systems. *Drug Saf* 2018;41:745-52.

**Table 1.** Characteristics of surgical patients with and without use of red yeast rice prescription

| | No RYR prescription (N=25810) | | RYR prescription (N=2581) | | |
|---|---|---|---|---|---|
| Baseline characteristics | n | (%) | n | (%) | p-value |
| Sex | | | | | 1.0000 |
| Female | 15500 | (60.1) | 1550 | (60.1) | |
| Male | 10310 | (39.9) | 1031 | (39.9) | |
| Age, years | | | | | 1.0000 |
| 20-29 | 750 | (2.9) | 75 | (2.9) | |
| 30-39 | 2870 | (11.1) | 287 | (11.1) | |
| 40-49 | 5570 | (21.6) | 557 | (21.6) | |
| 50-59 | 8130 | (31.5) | 813 | (31.5) | |
| 60-69 | 5630 | (21.8) | 563 | (21.8) | |
| 70-79 | 2450 | (9.5) | 245 | (9.5) | |
| ≥80 | 410 | (1.6) | 41 | (1.6) | |
| Low income | | | | | 0.7290 |
| No | 25159 | (97.5) | 2513 | (97.4) | |
| Yes | 651 | (2.5) | 68 | (2.6) | |
| Types of surgery | | | | | <0.0001 |
| Skin | 435 | (1.7) | 23 | (0.9) | |
| Breast | 626 | (2.4) | 76 | (2.9) | |
| Musculoskeletal | 7244 | (28.1) | 663 | (25.7) | |
| Respiratory | 1122 | (4.4) | 148 | (5.7) | |
| Cardiovascular | 721 | (2.8) | 60 | (2.3) | |
| Digestive | 5229 | (20.3) | 524 | (20.3) | |
| Kidney, ureter, bladder | 2110 | (8.2) | 253 | (9.8) | |
| Delivery, CS, abortion | 1272 | (4.9) | 87 | (3.4) | |
| Neurosurgery | 2672 | (10.4) | 312 | (12.1) | |
| Eye | 337 | (1.3) | 31 | (1.2) | |
| Others | 4042 | (15.7) | 404 | (15.7) | |
| Types of anesthesia | | | | | 0.0140 |
| General | 19241 | (74.6) | 1981 | (76.8) | |
| Epidural or Spinal | 6569 | (25.4) | 600 | (23.2) | |
| Number of hospitalizations | | | | | 0.1026 |
| 0 | 18859 | (73.1) | 1937 | (75.1) | |
| 1 | 4349 | (16.9) | 419 | (16.2) | |

| | | | | | |
|---|---|---|---|---|---|
| 2 | 1280 | (5.0) | 112 | (4.3) | |
| ≥3 | 1322 | (5.1) | 113 | (4.4) | |
| Number of emergency visits | | | | | 0.6529 |
| 0 | 16336 | (63.3) | 1633 | (63.3) | |
| 1 | 5495 | (21.3) | 570 | (22.1) | |
| 2 | 2119 | (8.2) | 203 | (7.9) | |
| ≥3 | 1860 | (7.2) | 175 | (6.8) | |
| Medical conditions | | | | | |
| Hypertension | 6022 | (23.3) | 890 | (34.5) | <0.0001 |
| Mental disorders | 4128 | (16.0) | 671 | (26.0) | <0.0001 |
| Diabetes | 3456 | (13.4) | 415 | (16.1) | 0.0001 |
| Ischemic heart disease | 1785 | (6.9) | 283 | (11.0) | <0.0001 |
| COPD | 925 | (3.6) | 108 | (4.2) | 0.1203 |
| Liver cirrhosis | 704 | (2.7) | 88 | (3.4) | 0.0449 |
| Heart failure | 417 | (1.6) | 49 | (1.9) | 0.2809 |
| Renal dialysis | 559 | (2.2) | 17 | (0.7) | <0.0001 |

COPD, chronic obstructive pulmonary disease; RYR, red yeast rice.

**Table 2.** Risk of postoperative complications and mortality in surgical patients with and without use of red yeast rice prescription

| | No RYR prescription (N=25810) | | RYR prescription (N=2581) | | Outcome risk |
|---|---|---|---|---|---|
| Postoperative outcomes | Events | % | Events | % | OR (95% CI)[a] |
| 30-day in-hospital mortality | 135 | 0.5 | 5 | 0.2 | 0.37 (0.15-0.92) |
| Complications | | | | | |
| Pneumonia | 452 | 1.8 | 24 | 0.9 | 0.54 (0.36-0.83) |
| Septicemia | 876 | 3.4 | 73 | 2.8 | 0.89 (0.70-1.14) |
| Pulmonary embolism | 17 | 0.1 | 5 | 0.2 | 3.30 (1.18-9.20) |
| Acute renal failure | 142 | 0.6 | 14 | 0.5 | 0.96 (0.55-1.69) |
| Stroke | 552 | 2.1 | 39 | 1.5 | 0.66 (0.47-0.92) |
| Urinary tract infection | 1129 | 4.4 | 130 | 5.0 | 1.09 (0.90-1.33) |
| Deep wound infection | 121 | 0.5 | 9 | 0.4 | 0.76 (0.38-1.51) |
| AMI | 63 | 0.2 | 3 | 0.1 | 0.48 (0.15-1.59) |
| Postoperative bleeding | 138 | 0.5 | 5 | 0.2 | 0.36 (0.15-0.89) |
| ICU stay | 2468 | 9.6 | 171 | 6.6 | 0.64 (0.54-0.77) |
| Postoperative adverse events[b] | 2983 | 11.6 | 206 | 8.0 | 0.63 (0.54-0.74) |
| Medical expenditure, USD[c] | 2709±3795 | | 2480±3271 | | p=0.0008 |
| Length of hospital stay, days[c] | 7.6±9.7 | | 6.1±7.1 | | p<0.0001 |

AMI, acute myocardial infarction; CI, confidence interval; OR, odds ratio; RYR, red yeast rice

[a]Adjusted for all covariates listed in Table 1.

[b] Adverse events included with 30-day in-hospital mortality, pneumonia, stroke, postoperative bleeding, and admitted to intensive care unit; After excluding those used statin within preoperative 24-months in RYR group (n=2491), the adjusted OR of RYR associated with postoperative adverse events was 0.62 (95% CI=0.53-0.73).

[c]Mean±SD; RYR prescription was associated with length of hospital stays (beta=-1.4, p<0.0001) and medical expenditure (beta=-247.9, p=0.0007) after adjusted all covariates listed in Table 1 in the multiple linear regressions.

**Table 3.** The stratified analysis for the association between red yeast rice prescription and postoperative adverse events

| | | | Adverse events[a] | | |
|---|---|---|---|---|---|
| | | n | Events | Rate, % | OR (95% CI)[b] |
| Female | No RYR | 15500 | 1363 | 8.8 | 1.00 (reference) |
| | RYR | 1550 | 87 | 5.6 | 0.57 (0.44-0.72) |
| Male | No RYR | 10310 | 1620 | 15.7 | 1.00 (reference) |
| | RYR | 1031 | 119 | 11.5 | 0.69 (0.55-0.86) |
| Age 20-39 years | No RYR | 3620 | 149 | 4.1 | 1.00 (reference) |
| | RYR | 362 | 12 | 3.3 | 0.73 (0.38-1.41) |
| Age 40-49 years | No RYR | 5570 | 445 | 8.0 | 1.00 (reference) |
| | RYR | 557 | 41 | 7.4 | 0.80 (0.55-1.15) |
| Age 50-59 years | No RYR | 8130 | 872 | 10.7 | 1.00 (reference) |
| | RYR | 813 | 55 | 6.8 | 0.63 (0.47-0.85) |
| Age 60-69 years | No RYR | 5630 | 852 | 15.1 | 1.00 (reference) |
| | RYR | 563 | 57 | 10.1 | 0.57 (0.41-0.78) |
| Age ≥70 years | No RYR | 2860 | 665 | 23.3 | 1.00 (reference) |
| | RYR | 286 | 41 | 14.3 | 0.59 (0.41-0.85) |
| 0 hospitalization | No RYR | 18859 | 1560 | 8.3 | 1.00 (reference) |
| | RYR | 1937 | 119 | 6.1 | 0.63 (0.52-0.78) |
| 1 hospitalization | No RYR | 4349 | 724 | 16.7 | 1.00 (reference) |
| | RYR | 419 | 57 | 13.6 | 0.76 (0.55-1.06) |
| ≥2 hospitalizations | No RYR | 2602 | 699 | 26.9 | 1.00 (reference) |
| | RYR | 225 | 30 | 13.3 | 0.44 (0.28-0.67) |
| 0 emergency visit | No RYR | 16336 | 1462 | 9.0 | 1.00 (reference) |
| | RYR | 1633 | 118 | 7.2 | 0.68 (0.55-0.84) |
| 1 emergency visit | No RYR | 5495 | 699 | 12.7 | 1.00 (reference) |
| | RYR | 570 | 45 | 7.9 | 0.60 (0.43-0.85) |
| ≥2 emergency visits | No RYR | 3979 | 822 | 20.7 | 1.00 (reference) |
| | RYR | 378 | 43 | 11.4 | 0.55 (0.38-0.79) |
| 0 medical condition | No RYR | 13535 | 1042 | 7.7 | 1.00 (reference) |
| | RYR | 951 | 63 | 6.6 | 0.80 (0.60-1.06) |
| 1 medical condition | No RYR | 8048 | 1061 | 13.2 | 1.00 (reference) |
| | RYR | 970 | 73 | 7.5 | 0.56 (0.43-0.74) |
| ≥2 medical conditions | No RYR | 4227 | 880 | 20.8 | 1.00 (reference) |
| | RYR | 660 | 70 | 10.6 | 0.53 (0.39-0.70) |

CI, confidence interval; OR, odds ratio; RYR, red yeast rice.

[a]Adverse events included with 30-day in-hospital mortality, pneumonia, stroke, postoperative bleeding, and admitted to intensive care unit.

[b]Adjusted for all covariates listed in Table 1.

**Table 4** Risk of postoperative adverse events associated with cumulative consumption of RYR capsules[a]

| Cumulative consumption of RYR, capsules | Adverse events after surgery | | | |
|---|---|---|---|---|
| | n | Events | Incidence,% | OR (95% CI)[b] |
| 0-90 | 1618 | 136 | 8.4 | 0.70 (0.57-0.85) |
| 91-180 | 385 | 26 | 6.8 | 0.63 (0.41-0.97) |
| ≥181 | 578 | 44 | 7.6 | 0.65 (0.47-0.91) |

CI, confidence interval; OR, odds ratio; RYR, Red Yeast Rice

[a]Daily recommended dose is 2 capsules and per capsule included RYR 600 mg; adverse events included with 30-day in-hospital mortality, pneumonia, stroke, postoperative bleeding, and admitted to intensive care unit.

[b]Adjusted for all covariates listed in Table 1.