

REVIEW ARTICLE

A Meta-Analysis of 80% Fraction of Inspired Oxygen on Surgical Site Infection in Patients Undergoing Surgery

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ABSTRACT

Background: WHO recommended the use of 80% FiO₂ in patients undergoing general anesthesia with endotracheal intubation (ETI) to prevent surgical site infection (SSI). However, the ongoing debate regarding efficacy and safety raises because further trials have been published. We conducted a review based on recommendations in terms of SSI as the primary outcome and adverse events as the secondary outcome in both patients with or without ETI.

Method: A literature search was carried out by PubMed, ScienceDirect, and Google Scholar for RCTs in all-type surgical patients who administrated 80% FiO₂ compared with 30–35% FiO₂. Pooled relative risks with a 95% confidence interval were conducted for meta-analysis.

Result: Based on 23 RCTs included in the analysis, there were no significant differences in terms of SSI (RR,0.85; 95%CI, 0.72 to 1.01; p=0.07), sepsis (RR,1.47; 95%CI, 0.78 to 2.76; p=0.23), postoperative hospitalization days (PHD) (RR,0.16; 95%CI, -0.67 to 0.98; p=0.71), ICU admission (RR,0.94; 95%CI, 0.78 to 1.13; p=0.50), reoperation required (RR,0.78; 95%CI, 0.30 to 2.06; p=0.62), and 30-days mortality (RR,1.18; 95%CI, 0.76 to 1.84; p=0.45). In contrast, even though the subgroup analysis showed association that PHD longer in high FiO₂ group for colorectal surgery (RR,0.80; 95%CI, 0.24 to 1.35; p=0.005), the high FiO₂ significantly reduced SSI and anastomotic leakage in abdominal surgery (RR,0.78; 95%CI, 0.62 to 0.99; p=0.04 and RR,0.55; 95%CI, 0.36 to 0.85; p=0.008).

Conclusion: This meta-analysis provides evidence that administration of 80% FiO₂ even though association with longer of PHD in colorectal surgery, it is associated with a reduction in SSI and anastomotic leakage in patients who underwent abdominal surgery. It contrasts for sepsis, ICU admission, reoperation required, 30-day mortality, SSI, and PHD in all-type surgery.

Keywords: adverse events; meta-analysis; oxygen; surgery; surgical site infection.



INTRODUCTION

Surgical site infections (SSI) are infection on incision site after surgery that clinically important postoperative adverse event because it leads to length of hospitalization, morbidity, mortality, and increases a considerable cost on health care system^{1,2}. A total of 135 from 4,893 (2.8%) abdominal surgeries developed SSI has been reported at Cipto Mangunkusumo Hospital, Jakarta, Indonesia, from January 2012 to November 2017³. Preventive strategies approach by surgical or anesthesia departments to overcome this condition were urgently needed in order to enhanced satisfactory surgical care system. World Health Organization (WHO) have recommendation the use of 80% Fraction of inspiratory oxygen (FiO₂) as perioperative strategy to reduce the risk or incidence of surgical site infection in adult patients with endotracheal tube intubation under general anesthesia⁴. High concentrations of inspired oxygen might increase tissue oxygenation and thereby enhancing oxidative killing by neutrophil as bactericidal host defence. This mechanism is mediated when the superoxide anion is converted to hydrogen peroxide and then catalyzed by

myeloperoxidase into hypochlorous acid which has a bactericidal mechanism⁵. Recent meta-analysis showed that 80% fraction of inspiratory oxygen clinically safe to reduce SSI in patients undergoing surgery and no substantial of safety concern against WHO recommendations⁶. However, further studies were widely published still lead to ongoing debate over the clinical use of high fraction of inspiratory oxygen. We conducted a review based on WHO recommendations in terms of surgical site infection as the primary outcome and adverse events such as sepsis, postoperative hospitalization days (PHD), anastomotic leakage, reoperation required, and 30-days mortality as the secondary outcome in both patients with or without endotracheal intubation.

METHODS

This systematic review and meta-analysis was reported based on the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) guideline⁷.

Database Searching and Study Selection

We performed database literature searching in Pubmed, Google Scholar, and ScienceDirect using the following

keywords: Oxygen, FiO₂, (Surgical Site Infection OR SSI), and Surgery.

We only included articles that match our eligibility criteria: (1) Reported patients who underwent a major surgery aged 18 year or older; (2) The patients received an intervention either high FiO₂ (80%) or low FiO₂ (30-35%); (3) Reported at least one of the following outcomes: Surgical site infection (SSI), sepsis, anastomotic leakage, postoperative hospitalization days (PHD), ICU admission, reoperation, and 30-days mortality; (4) The article used RCT study design; (5) Written in English. The literature search was done in February 2022 without any year restriction.

All results from the databases were inputted in *Rayyan.ai*, an artificial intelligence online program that integrated to expedite the initial screening of abstracts and titles during studies selection process⁸. Two independent reviewers (RNE and AIT) selected the articles based on title and abstracts.

All articles that passed the title and abstract selection were screened for the eligibility criteria. Any conflicts in articles within the article selection were discussed with all authors.

Data extraction

All included studies underwent data extraction by two independent reviewers (RNE and AIT). The main outcome of this study is SSI. There were many secondary outcomes such as the incidence of sepsis, anastomotic leakage, PHD, ICU admission, reoperation, and mortality. Several data were extracted from the studies including the author, year, sample size, age, type of surgery, duration of surgery, outcome, type of anesthesia, postoperative oxygenation, follow-up, and bacterial culture. Any controversies between data extraction were discussed with other authors.

Risk of bias assessment

The risk of bias in each study was assessed using Cochrane Risk of Bias 2 (ROB 2) tool⁹. The ROB 2 tool consists of five domains like selection bias, performance bias, detection bias, attrition bias, and reporting bias. Each domain was graded as “low risk”, “some concern”, and “high risk” of bias.

The risk of bias assessment was conducted by two authors (LI and YTS) independently. Any difference in terms of grading was discussed with other authors. Publication bias was assessed using a funnel plot if only there were 10 or more studies included in the analysis,

a symmetrical funnel plot is defined as low publication bias.

Data synthesis and analysis

The data were analyzed both analyzed narratively and quantitatively using meta-analysis. The meta-analysis was conducted using Review Manager (RevMan) 5.4 (Cochrane collaboration, oxford, UK) with 95% confidence interval (CI). Pooled risk ratio was used to calculate the outcome of SSI, sepsis, anastomotic leakage, ICU admission, reoperation, and mortality.

In addition, pooled mean difference (MD) was used to calculate the outcome in PHD. Random Effects Model (REM) and Fixed Effects Model (FIM) were used based on the heterogeneity ($I^2 > 50\%$ determined as high heterogeneity, $I^2 < 50\%$ determined as low heterogeneity) based on Cochrane handbook of systematic reviews of interventions¹⁰. A subgroup analysis was performed based on the type of surgery.

RESULTS

Studies Selection

Based on the database searching, we found a total of 1954 articles from Pubmed, Google Scholar, and ScienceDirect. We conducted the duplicate screening automatically using Rayyan.ai and then underwent title and

abstract screening. After title and abstract screening, 25 articles were checked for eligibility by full-text screening. Qualitative synthesis and quantitative analysis using meta-analysis were performed in 23 included articles. Figure 1 shows the PRISMA flow chart.

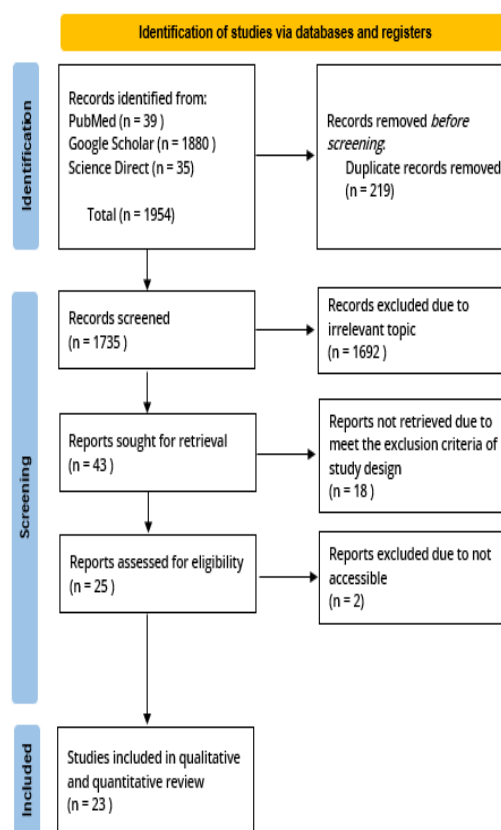


Figure 1. PRISMA Flowchart

Study characteristics and Risk of Bias

Table 1 and Table 2 summarize all the included RCT studies. The sample size varied between each study ranging from 38 to 2012 samples. The included studies were conducted in several countries such as Austria¹, USA⁶, Spain¹, Israel², Denmark¹, France¹, Hong Kong¹,

Italy³, India², Iran¹, China¹, and multicenter countries³.

The risk of bias assessment was conducted using Cochrane ROB 2 tool and presented in supplementary files.

The risk of bias varied from low risk – high risk of bias. There are 7 studies labeled as low risks of bias, 8 studies some concern/uncertain, and 8 studies high risks of bias.

Table 1. Characteristic of included studies part 1

| Study | Sample Size | Type of surgery | Age | | Duration of surgery | | Intervention | | Patients outcomes |
|--|-------------|--|-----------------------|----------------------|-----------------------|----------------------|--|--|--|
| | | | High FiO ₂ | Low FiO ₂ | High FiO ₂ | Low FiO ₂ | High FiO ₂ | Low FiO ₂ | |
| Greif et al, (2000) Austria ¹¹ | 500 | Elective open colorectal resection | 57±15 | 57±15 | 3.1±1.4 (h) | 3.1±1.4 (h) | 80% O ₂ with 20% N ₂ O | 30% O ₂ with 70% N ₂ O | SSI, PHD, ICU admission |
| Pryor et al, (2004) USA ¹² | 160 | Major abdominal surgery | 54±16 | 57±15 | 233±83 (min) | 208±91 (min) | 80% O ₂ | 35% O ₂ | SSI, PHD, ICU admission |
| Belda et al, (2005) Spain ¹³ | 291 | Elective colorectal resection | 64.2±11.8 | 62.3±12.5 | 161±62 (min) | 159±61 (min) | 80% O ₂ | 30% O ₂ | SSI, PHD, ICU admission |
| Mayzler et al, (2005) Israel ¹⁴ | 38 | Elective colorectal surgery | 67±10 | 69±9 | 140±40 (min) | 135±40 (min) | 80% O ₂ with 20% N ₂ O | 30% O ₂ with 70% N ₂ O | SSI, anastomotic leakage |
| Myles et al, (2007) Multicenter ¹⁵ | 2012 | Mixed surgeries | 55.8±17 | 54.6±16 | 3.3±2.0 (h) | 3.3±2.0 (h) | 80% O ₂ with 20% N ₂ O | 30% O ₂ with 70% N ₂ O | SSI, ICU admission, 30-days mortality |
| Gardella et al, (2008) USA ¹⁶ | 143 | Caesarean section | 31 (19–46) | 28 (16–47) | 48 (26–87) (min) | 52 (20–141) (min) | 80% O ₂ | 30% O ₂ | SSI |
| Meyhoff et al, (2009) Denmark ¹⁷ | 1386 | Acute or elective laparotomy | 64 (27–85) | 64 (34–84) | 128 (38–310) (min) | 132 (35–295) (min) | 80% O ₂ | 30% O ₂ | SSI, ICU admission, anastomotic leakage, PHD, re 30-days mortality |
| | 633 | Colorectal surgery | NR | NR | NR | NR | 80% O ₂ | 30% O ₂ | SSI |
| Bickel et al, (2011) Israel ¹⁸ | 210 | Open appendectomy | 28.5±12.3 | 27.6±10.8 | 33.04±10.6 (min) | 32.75±10.3 (min) | 80% O ₂ with 20% air | 30% O ₂ with 70% N ₂ O | SSI, PHD |
| Scifres et al, (2011) USA ¹⁹ | 585 | Caesarean section | 27.5±6.4 | 27.8±5.9 | 57.4±20.5 (min) | 60.6±26.1 (min) | 80% O ₂ | 25–35% O ₂ | SSI |
| Thibon et al, (2012) France ²⁰ | 434 | Abdominal, gynecologic, breast (Mixed surgeries) | 52.1±13.7 | 51.8±13.3 | 89±61 (min) | 84±58 (min) | 80% O ₂ | 30% O ₂ | SSI |
| Chen et al, (2013) Hong Kong ²¹ | 60 | Open colorectal surgery | 62±12 | 60±15 | A/199±76 (min) | A/184±85 (min) | 80% O ₂ | 30% O ₂ | SSI, PHD |
| Duggal et al, (2013) USA ²² | 831 | Caesarean section | 29.2±5.6 | 29.5±5.8 | NR | NR | 80% O ₂ | 30% O ₂ | SSI and/or endometritis |
| Schietroma et al, (2013) Italy ²³ | 171 | gastrectomy and subsequent esophagojejunal anastomosis | 68.4 (51–84) | 67.8 (48–82) | 175 (100–250) (min) | 180 (118–270) (min) | 80% O ₂ | 30% O ₂ | SSI, anastomotic leakage, reoperation required |
| Stall et al (2013) USA ²⁴ | 235 | Open reduction and internal fixation | 42.3±12.1 | 42.5±12.2 | 233±88 (min) | 228±88 (min) | 80% O ₂ | 30% O ₂ | SSI |
| Williams et al, (2013) USA ²⁵ | 160 | Caesarean section | 24.6024 | 24.8961 | 51.2048 (min) | 52.2467 (min) | 80% O ₂ | 30% O ₂ | SSI |
| Kurz et al, (2015) Multicenter ²⁶ | 586 | Colorectal resection | 54±16 | 51±17 | 3.5±1.5 (h) | 3.5±1.8 (h) | 80% O ₂ | 30% O ₂ | SSI, PHD, 30-days mortality |
| Wasnik et al, (2015) India ²⁷ | 64 | Open Appendectomy | 27.15±10.46 | 28.56±12.22 | 61.87±10.6 (min) | 61.4±12.5 (min) | 80% O ₂ | 30% O ₂ | SSI, PHD |
| Fariba et al, (2016) Iran ²⁸ | 122 | Caesarean section | 29.70±5.4 | 29.26±4.6 | 57.5±14.2 (min) | 60±10.4 (min) | 80% O ₂ | 30% O ₂ | SSI |
| Schietroma et al, (2016a) Italy ²⁹ | 239 | Open perforated peptic ulcer surgery | 58.3 (35–80) | 57.8 (30–82) | 63.2 (38–104) min | 58.7 (33–102) min | 80% O ₂ | 30% O ₂ | SSI |
| Schietroma et al, (2016b) Italy ³⁰ | 85 | Open colorectal resection | 71.4 (55–92) | 68.6 (49–86) | 200 (95–410) min | 195 (100–385) min | 80% O ₂ | 30% O ₂ | SSI, anastomotic leakage, reoperation required |
| Mayank et al, (2019) India ³¹ | 94 | Elective colorectal surgery | 57.02±12.94 | 53.36±14.45 | 233.51±87.65 (min) | 207.66±103.53 (min) | 80% O ₂ with 20% N ₂ O | 33% O ₂ with 66% N ₂ O | SSI, PHD, anastomotic leakage |
| Ferrando et al, (2020) Multicenter ³² | 740 | Abdominal sutgery | 64.2±12.8 | 63.9±13.9 | 214.2±93.3 (min) | 209.2±89.7 (min) | 80% O ₂ | 30% O ₂ | SSI, PHD, 30-days mortality |
| Xue-Fei Li et al, (2020) China ³³ | 251 | Abdominal surgery | 54±14 | 53±13 | 190 (154–245) min | 200 (146–258) min | 80% O ₂ | 30% O ₂ | SSI, sepsis, ICU admission |

SSI= surgical site infection; PHD= postoperative hospitalization days; ICU= intensive care unit; min= minutes; h= hour

Table 2. Characteristic of included studies part 2

| Study | Type of SSI Assessment | Type of anaesthesia | Post-operative oxygenation | Follow up for SSI assesment | Bacterial culture |
|--|--|----------------------|--|-----------------------------|--|
| Greif et al (2000) Austria ¹¹ | ASEPSIS scores | General | 2 h by NRBM | 15 days | <i>Escherichia coli</i> Enterococcus <i>Pseudomonas aeruginosa</i> <i>Staphylococcus aureus</i> <i>S. epidermidis</i> Enterobacter |
| Pryor et al, (2004) USA ¹² | NR | General | 2 h by CN for low group and NRBM for high group | 14 days | <i>Escherichia coli</i> <i>Bacteroides fragilis</i> <i>Enterococcus faecalis</i> Coagulase-negative staphylococcus No species identified |
| Belda et al, (2005) Spain ¹³ | ASEPSIS scores and CDC criteria | General | 6 h by NRBM | 14 days | NR |
| Mayzler et al, (2005) Israel ¹⁴ | NR | General | 2 h by face mask | 30 days | NR |
| Myles et al, (2007) Multicenter ¹⁵ | NR | General | NR | 30 days | NR |
| Gardella et al, (2008) USA ¹⁶ | NR | Regional | 2 h by NRBM | 14 days | Group B streptococcus |
| Meyhoff et al, (2009) Denmark ¹⁷ | ASEPSIS scores and CDC criteria | General | 2 h by NRBM | 14 days | NR |
| Bickel et al, (2011) Israel ¹⁸ | ASEPSIS scores | General | 2 h by CN for low group and NRBM for high group | 14 days | NR |
| Scifres et al, (2011) USA ¹⁹ | NR | Regional | 2 h by CN for low group and NRBM for high group | 28 days | Group B streptococcus |
| Thibon et al, (2012) France ²⁰ | CDC criteria | General | NR | 30 days | <i>Staphylococcus aureus</i> coagulasenegative staphylococcal species <i>Pseudomonas aeruginosa</i> Gram-negative bacteria |
| Chen et al, (2013) Hong Kong ²¹ | ASEPSIS scores and CDC criteria | General | 24 h by facemask | 30 days | NR |
| Duggal et al, (2013) USA ²² | NR | Regional | 1 h by facemask | 14 days | NR |
| Schietroma et al, (2013) Italy ²³ | NR | General | 6 h by facemask with reservoir | NR | NR |
| Stall et al, (2013) USA ²⁴ | ASEPSIS scores and CDC criteria | General | 2 h by CN for low group and NRBM for high group | 12 weeks | NR |
| Williams et al, (2013) USA ²⁵ | CDC criteria | Regional | 2 h by aerosol mask | 6 weeks | NR |
| Kurz et al, (2015) Multicenter ²⁶ | CDC criteria | General | 1 h by NRBM | 30 days | NR |
| Wasnik et al, (2015) India ²⁷ | ASEPSIS scores | NR | 2 h | 10 days | NR |
| Fariba et al, (2016) Iran ²⁸ | ASEPSIS scores | Regional | 6 h by normal mask for low group and venturi mask for high group | 14 days | NR |
| Schietroma et al, (2016a) Ital ²⁹ | ASEPSIS scores and CDC criteria | General | 6 h by NRBM with a reservoir | 14 days | NR |
| Schietroma et al, (2016b) Italy ³⁰ | NNIS, SENIC scales, and ASEPSIS scores | General | 6 h by NRBM | 14 days | NR |
| Mayank et al, (2019) India ³¹ | ASEPSIS score and CDC criteria | General | 6 h by standard venturi mask for low group and NRBM venturi face mask for high group | 2 days | NR |
| Ferrando et al, (2020) Multicenter ³² | CDC criteria | General and Regional | 3 h by venturi mask for low group and NRBM with a reservoir for high group | 30 days | NR |
| Xue-Fei Li et al, (2020) China ³³ | CDC criteria | General | NR | 7 days | NR |

NR= Not Reported; h= hour; CN= canule nasal; NRBM= non rebreathable mask

Outcomes: Surgical site Infection

23 studies reported on surgical site infection incidences with 656/4672 events in the low FiO₂ and 558/4671 events in the high FiO₂ (Figure 2).

Overall, high FiO₂ was not associated with an reducing risk of SSI in all-type surgery (pooled RR 0.85; 95% CI 0.72 – 1.01; p=0.07). There was considerable heterogeneity in the analysis (I²=52%).

Accordance results also showed by subgroup analysis revealed that high FiO_2 statistically no significant to reduced SSI for colorectal surgery (pooled RR 0.84; 95% CI 0.64 – 1.10; $p=0.20$), open appendectomy (pooled RR 0.41; 95% CI 0.16 – 1.03; $p=0.06$), and caesarean section (pooled RR 1.20; 95% CI 0.91 – 1.58; $p=0.21$).

In contrast, high FiO_2 significantly reduced SSI in patients who underwent abdominal surgery (pooled RR 0.78; 95% CI 0.62 – 0.99; $p=0.04$) with high heterogeneity between studies ($I^2=61\%$).

Outcomes: Sepsis

Two studies reported on sepsis with 16/826 events in low FiO_2 and 23/811 events in high FiO_2 .

This results showed the trend of sepsis higher in high FiO_2 group but the pooled estimates did not demonstrate statistically significant (pooled RR 1.47; 95% CI 0.78 – 2.76; $p=0.23$). There was mild heterogeneity ($I^2=0\%$).

Outcomes: Anastomotic leakage

Anastomotic leakage only available for abdominal surgery and conducted by six trials with 51/466 events in low FiO_2 and 28/464 in high FiO_2 (Figure 3). The pooled estimates showed that high FiO_2 statistically

significant in terms to reducing the incidence of anastomotic leakage for abdominal surgery (pooled RR 0.55; 95% CI 0.36 – 0.85; $p=0.008$).

Low heterogeneity was observed in the analysis ($I^2=0\%$).

Four studies conducted for colorectal surgery as subgroup analysis showed statistically significant association between high FiO_2 and anastomotic leakage (pooled RR 0.61; 95% CI 0.37 – 1.00; $p=0.05$). Heterogeneity between studies was low ($I^2=0\%$).

Outcomes: Postoperative hospitalization days

Eight studies reported on postoperative hospitalization days (PHD) available only for abdominal surgery. The result showed not significantly differing between the groups (pooled MD 0.16; 95% CI -0.67 – 0.98; $p=0.71$). Heterogeneity between studies was high ($I^2=0.74$).

Subgroup analysis was conducted in terms for open appendectomy showed no significantly differing (pooled MD -1.25; 95% CI -3.23 – 0.74; $p=0.22$) with high heterogeneity ($I^2=80\%$). However, instead reducing the PHD for colorectal surgery as subgroup analysis, high FiO_2

showed statistically significant increase (p=0.005). A low heterogeneity of PHD (pooled MD 0.80; 95% CI 0.24 – 1.35; p=0.005). A low heterogeneity was observed ($I^2 = 0\%$).

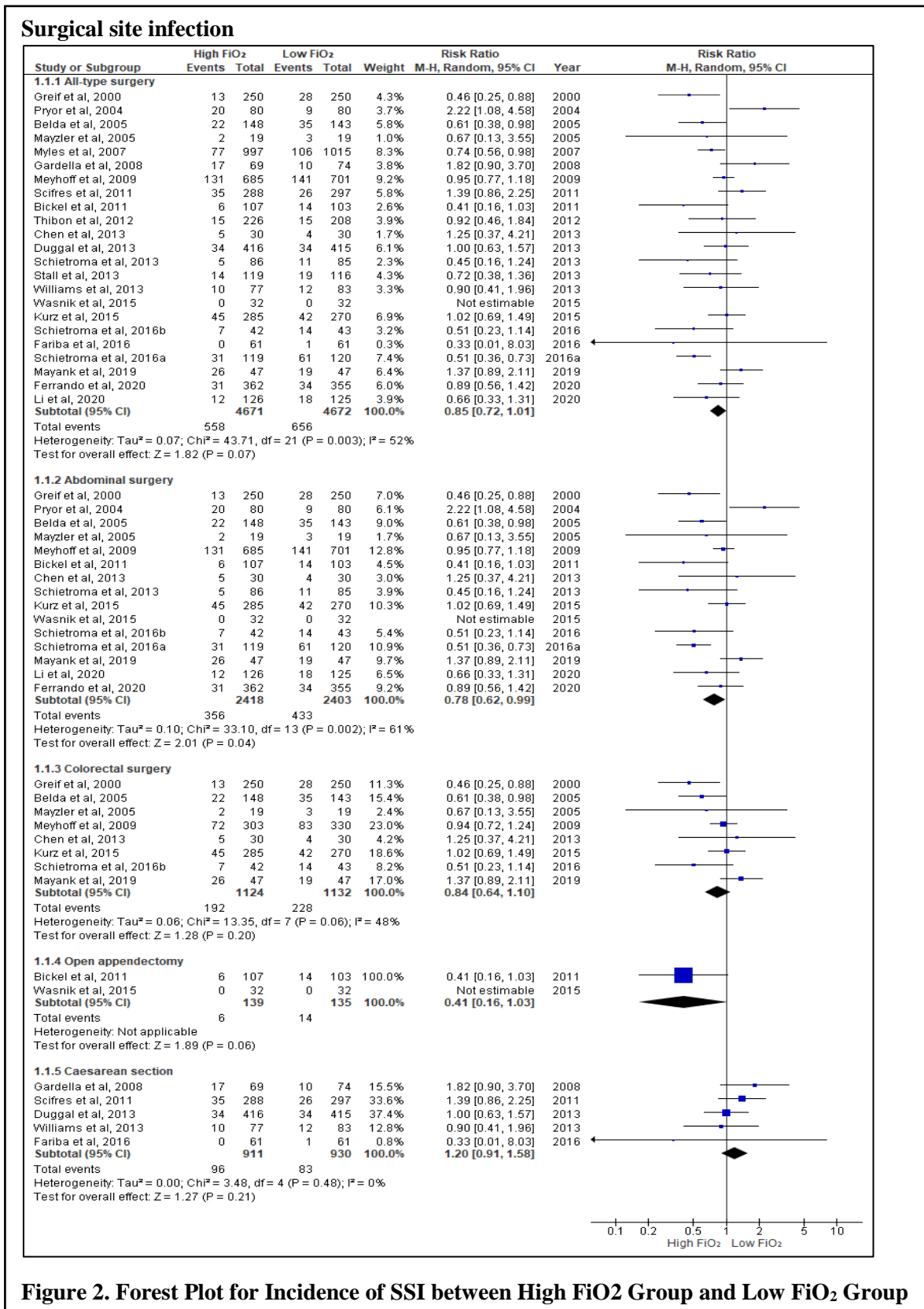
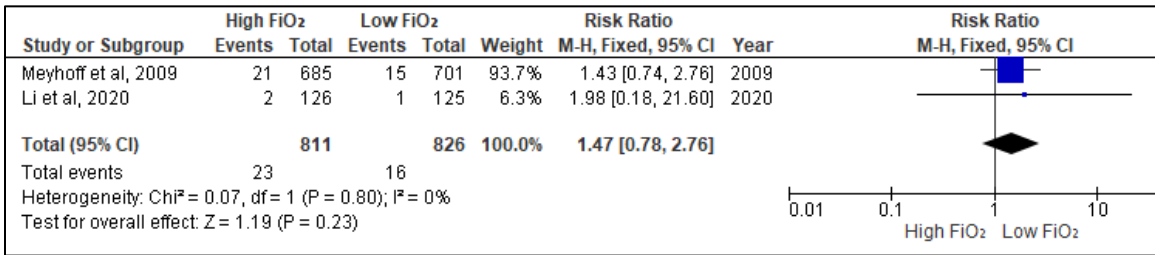
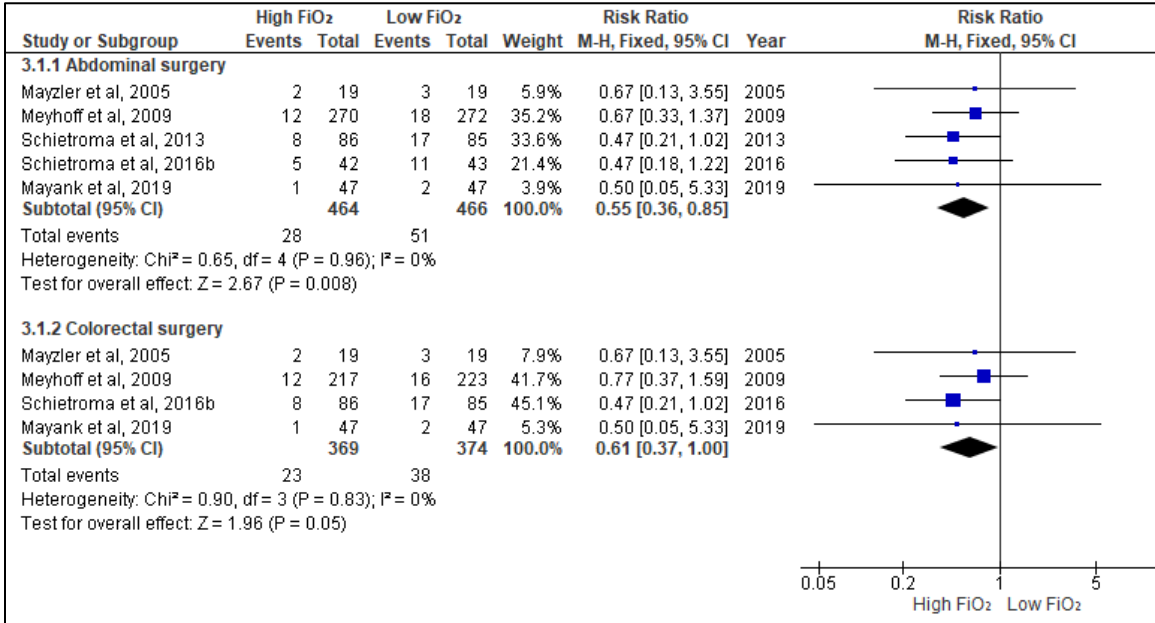


Figure 2. Forest Plot for Incidence of SSI between High FiO₂ Group and Low FiO₂ Group

a) Sepsis



b) Anastomotic leakage



c) Postoperative hospitalization days

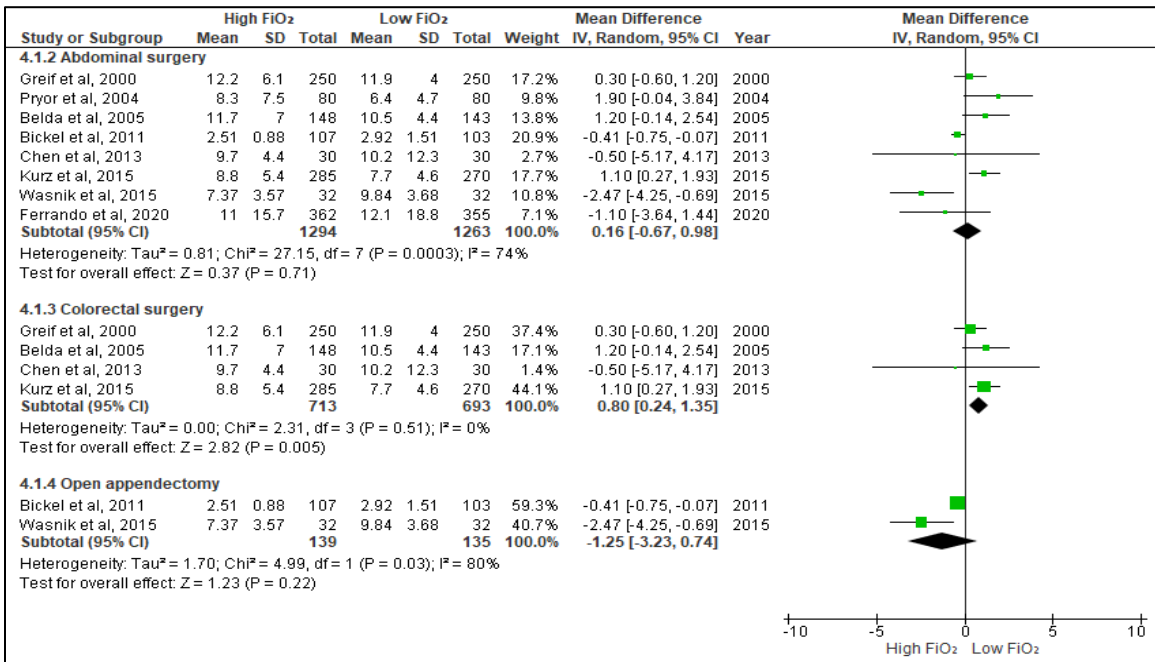
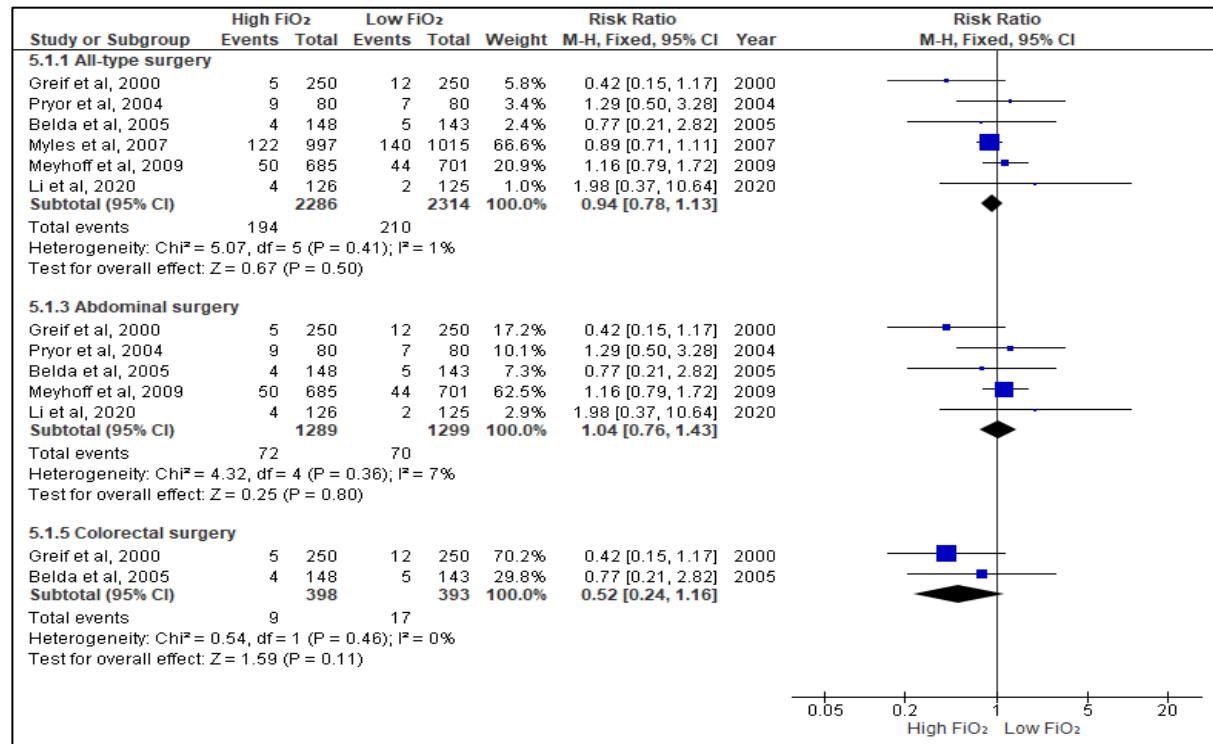
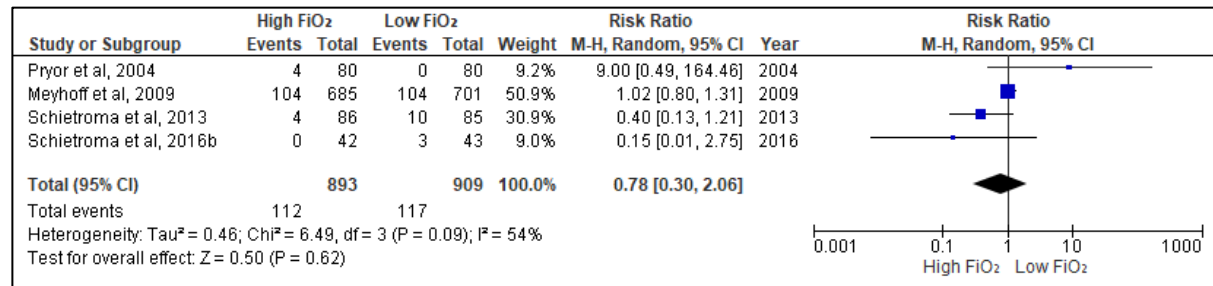


Figure 3. Forest Plot for Incidence of Sepsis, Anastomotic leakage, and Postoperative hospitalization days between High FiO₂ Group and Low FiO₂ Group

d) ICU Admission



e) Reoperation required



f) 30-days mortality

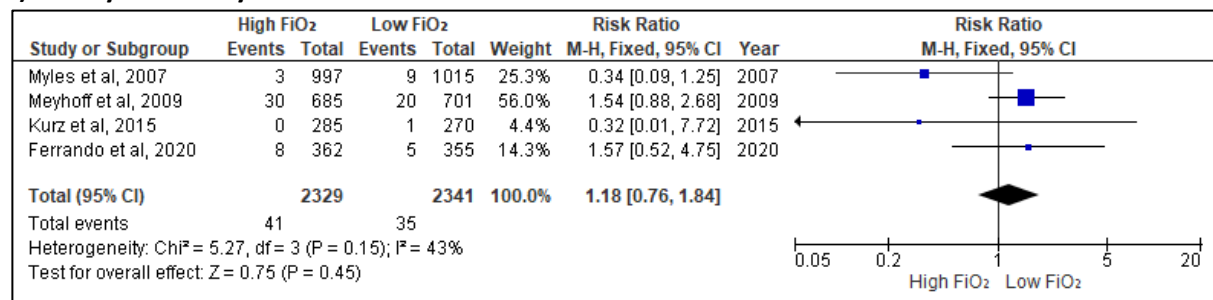


Figure 4. Forest Plot for ICU Admission, Reoperation Required, and 30-days mortality between High FiO₂ Group and Low FiO₂ Group

Outcomes: ICU admission

Six studies reported on ICU admission with 210/2314 patients in low

FiO₂ group and 194/2286 in high FiO₂ group. There was statistically no significant in terms of ICU admission for

all-type surgery between the groups (pooled RR 0.94; 95% CI 0.78 – 1.13; $p=0.50$) with low heterogeneity was observed ($I^2=1\%$). The subgroup analysis was conducted for abdominal surgery and colorectal surgery also showed statistically no significant difference (pooled RR 1.04; 95% CI 0.76 – 1.43; $p=0.80$) and (pooled RR 0.52; 95% CI 0.24 – 1.16; $p=0.11$) with low heterogeneity was observed ($I^2=7\%$) and ($I^2=0\%$).

Outcomes: Reoperation required

Four studies reported on reoperation required, where of 117/909 events observed in the low FiO_2 group and 112/893 events in the high FiO_2 group. There was no significant difference in the reoperation required between the groups (pooled RR 0.78; 95% CI 0.30 – 2.06; $p=0.62$). High heterogeneity was observed in the analysis ($I^2=54\%$).

Outcomes: 30-days mortality

Four studies reported on 30-days mortality with 35/2341 events in the low FiO_2 group and 41/2329 events in the high FiO_2 group. 30-days mortality was observed higher in High FiO_2 group, but there was no statistically significant different (pooled RR 1.18; 95% CI 0.76

– 1.84; $p=0.45$). A low heterogeneity was observed ($I^2=43$).

DISCUSSION

A meta analysis of 23 RCTs involving 9,343 patients was conducted in both patients with or without endotracheal intubation in order to developing the WHO guideline. This study showed no evidence for a benefit of the use high FiO_2 (80%) compared low FiO_2 (30-35%) to prevent or reducing the risk of SSI in all-type surgery although the incidence of SSI was higher in low FiO_2 group. In contrast, previous meta-analysis similar with WHO guideline revealed that high FiO_2 reducing the SSI risk in surgical patients under general anaesthesia with endotracheal intubation^{4,34}. Although there are six additional studies where of three studies are the most recent³¹⁻³³ and three other are studies that have done of investigation enhanced that incidence of SSI still higher in low FiO_2 group, there are six studies showed contradictory incidence with relatively greatest RR than in other seventeen studies^{12,16,19,21,26,31}. Subgroup analysis in terms of colorectal surgery also showed no evidence benefit of the use high FiO_2 compared low FiO_2 , this results similar with previous meta analysis even though

these previous study was conducted not only for RCTs³⁵. Caesarean section and appendectomy that performed by a lack of included studies demonstrate that high FiO₂ no evidence for benefit to prevent SSI. However, modification of subgroup analysis performed for all-type abdominal surgery suggest that high FiO₂ beneficially to prevent or reducing the risk of SSI.

Instead reducing the postoperative adverse events, this meta analysis showed that the trend of sepsis and 30-days mortality was higher in high FiO₂ group even though the results no statistically significant. PHD only showed statistically significant in subgroup analysis in term for colorectal surgery revealed that the use of high FiO₂ increases duration of PHD. Previous meta-analysis showed no definite signal of harm with 80% FiO₂ in surgical patients undergoing general anaesthesia because of there is lack of safety-related included studies that suggest to discourage this perioperative treatment⁶. Supplementation of high and low FiO₂ did not differentially of the mortality, pneumonia, respiratory failure, and length of hospital stay, but high FiO₂ associated with a significantly higher incidence of atelectasis^{6,36}.

The incidence of ICU admission and reoperation required was higher in low FiO₂ group but did not statistically significant. The beneficially evidence of high FiO₂ for secondary outcomes was observed only for anastomotic leakage in terms of both abdominal surgery and colorectal surgery. This results contrasts with previous meta-analysis where of the included studies conducted by multiple study design³⁵. The beneficially of high FiO₂ for anastomotic leakage may related with increases of tissue perfusion in order to maintained mechanical stability of anastomosis³⁷.

Our meta-analysis was carry out by the most up to date search of the literature and clinically-important outcomes. However, this study has some limitations. First, the subgroup analysis performed by type of surgery instead of patient who undergo endotracheal intubation or not. However, there are no previous meta analysis that performed by type of surgery especially to investigated the use of high FiO₂ to reducing or prevent incidence of SSI. Second, the time of literature search not limited to the last 5 years, this condition was performed following WHO guideline which is the WHO latest guideline conducted by meta-analysis studies that

included studies above 5 years of publication.

CONCLUSION

In conclusion, the administration of 80% FiO₂ in both patients with or without endotracheal intubation for all-type surgery is not associated with the incidence of SSI, sepsis, PHD, ICU admission, reoperation required, and 30-days mortality. The evidence for a benefit the use of 80% FiO₂ is associated with reduction of SSI in abdominal surgery. It also showed beneficially for reducing of anastomotic leakage in abdominal and colorectal surgery. However, the use of 80% FiO₂ increases the duration of PHD in abdominal surgery.

In conclusion, based on the evidence showed in this result, the administration of 80% FiO₂ in both patients with or without endotracheal intubation is strongly associated with reduction of SSI in abdominal surgery. This intervention is also associated with the reduction of anastomotic leakage in abdominal and colorectal surgery. However, it increases the duration of PHD in abdominal surgery.

CONFLICT OF INTEREST

All authors declare no conflict of interest.

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