# ANESTHESIOLOGY

# **Supplemental Intraoperative Oxygen and Long-term Mortality**

# Subanalysis of a Multiple Crossover **Cluster Trial**

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**C** urgical site infections and wound-related complications Jare common and serious. While the overall incidence of surgical site infections is 1 to 3%,<sup>1-3</sup> it is 10% or more after colorectal surgery.<sup>4-6</sup> The primary defense against bacterial infection is oxidative killing by neutrophils, which requires molecular tissue oxygen.7 Increasing inspired oxygen is an easy and effective way to augment tissue oxygen.<sup>8,9</sup> The theory that supplemental oxygen might reduce the risk of surgical wound infection led to two decades of studies. While initial trials were supportive,<sup>9,10</sup> subsequent large trials were not,<sup>11,12</sup> and a recent meta-analysis of reliable trials suggests that supplemental oxygen at most slightly reduces the perioperative infection risk.<sup>13</sup>

The second largest trial of supplemental oxygen (Supplemental Oxygen and Complications After Abdominal Surgery [PROXI] trial; n = 1,400) by Meyhoff et al. reported that 80% inspired oxygen did not decrease the incidence of wound infections,<sup>11</sup> but increased the hazard for mortality by 30% over a median of 2.3 postoperative yr.14 Curiously, increased mortality was restricted to cancer patients.14 Postulated explanations include increased tumor growth as a result of hyperoxia-induced neovascularization, increased erythropoietin release, and DNA damage by oxygen-triggered reactive oxygen species.<sup>15-19</sup> However, further analysis of the PROXI trial revealed that new or recurrent cancers occurred at similar rates in patients given 30% and 80% oxygen.<sup>20</sup> Although new or recurrent cancers occurred slightly earlier in patients given 80% oxygen, the magnitude was insufficient to explain the excess mortality in the

# ABSTRACT

Background: Whether supplemental oxygen worsens long-term mortality remains unclear, with contradictory trial results. The authors therefore tested the hypothesis that supplemental oxygen (80% vs. 30%) increases the hazard for long-term mortality.

Methods: The authors conducted a post hoc analysis of a large multiple crossover cluster trial in which more than 5,000 colorectal surgeries on 4,088 adults were allocated to receive either 30% or 80% inspired oxygen during general anesthesia. The authors assessed the effect of 80% versus 30% target-inspired oxygen on long-term mortality and calculated Kaplan-Meier g survival estimates. Analysis was restricted to patients with a home address in Ohio because the authors could obtain reliable vital status information from the Ohio Department of Health (Columbus, Ohio) for them.

Results: A total of 3,471 qualifying colorectal surgeries performed in E 2,801 patients were analyzed, including 1,753 (51%) surgeries in 1,577 patients given 80% oxygen and 1,718 surgeries in 1,551 patients given 30% oxygen. The observed incidence of death after a median of 3 yr was 13% (234 of 1,753) in the 80% oxygen group and 14% (245 of 1,718) in the 30% oxygen group and 14% oxygen group. The estimated hazard ratio for mortality was 0.94 (95% Cl, 0.78 to 1.13; *P* = 0.493).

Conclusions: In this post hoc analysis of a large, controlled trial, suppleiology/article-pdf/134/5/709/511655/20210500.0-00013.pdf by mental oxygen did not increase postoperative mortality.

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## EDITOR'S PERSPECTIVE

#### What We Already Know about This Topic

• It remains unclear whether supplemental intraoperative oxygen (80% vs. 30%) worsens postoperative mortality.

#### What This Article Tells Us That Is New

• In a post hoc analysis of a controlled trial of 3,471 colorectal surgeries, the incidence of death after a median of 3 yr of follow-up geries, the incidence of death after a median of 3 yr of follow-up geries, the incidence of death after a median of 3 yr of follow-up geries, the incidence of death after a median of 3 yr of follow-up geries, the incidence of death after a median of 3 yr of follow-up geries, the incidence of death after a median of 3 yr of follow-up geries, the incidence of death after a median of 3 yr of follow-up geries, the incidence of death after a median of 3 yr of follow-up geries, the incidence of death after a median of 3 yr of follow-up geries, the incidence of death after a median of 3 yr of follow-up geries, the incidence of death after a median of 3 yr of follow-up geries, the incidence of death after a median of 3 yr of follow-up geries, the incidence of death after a median of 3 yr of follow-up geries, the incidence of death after a median of 3 yr of follow-up geries, the incidence of death after a median of 3 yr of follow-up geries, the incidence of death after a median of 3 yr of follow-up geries, the incidence of death after a median of 3 yr of follow-up geries, the incidence of death after a median of 3 yr of follow-up geries, the incidence of the incidence o

80% oxygen group. In contrast, a reanalysis of several trials showed virtually identical long-term mortality rates over median follow-up periods ranging from 4.3 yr to 12.8 yr in 927 patients who were randomized to 30% or 80% intraoperative oxygen.21

The extent to which supplemental oxygen might promote long-term mortality therefore remains unclear. By far the largest controlled trial of supplemental oxygen enrolled 4,088 patients who had 5,167 surgeries from January 2013

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to March 2016.<sup>12</sup> Sufficient time has now elapsed to reliably estimate long-term mortality in participating patients. We therefore tested the primary hypothesis that supplemental oxygen (80% *vs.* 30%) increases the risk of long-term mortality. Secondarily, we evaluated whether the effect of supplemental oxygen on long-term mortality differs in patients who did and did not have colorectal cancer.

#### **Materials and Methods**

We conducted a *post hoc* analysis of a large, single-center multiple crossover cluster trial in which adults having colorectal surgery were allocated to receive either 30% or 80% inspired oxygen ( $FIO_2$ ) during general anesthesia. In the original trial, we tested the primary hypothesis that supplemental oxygen (80% *vs.* 30% as tolerated) reduces the risk of a 30-day collapsed composite (one or more) of surgical site infection, healing-related wound complications, and mortality. The underlying trial was approved by the Cleveland Clinic Institutional Review Board (12-891; Cleveland, Ohio) with a waived requirement for informed consent and was registered at ClinicalTrials.gov (NCT01777568) on January 29, 2013. The principal investigator for registration was Andrea Kurz.

The current subanalysis was also approved with a waived requirement for informed consent by the Cleveland Clinic Institutional Review Board. A detailed statistical analysis plan was developed *a priori* and approved by the Cleveland Clinic Institutional Review Board. The primary outcome and several subanalyses from the original trial have been published, all focused on short-term outcomes.<sup>22–24</sup> The statisticians were not blinded to treatment group assignment.

In brief, all patients who had surgery in a designated operating room suite at the Cleveland Clinic Main Campus (Cleveland, Ohio) over a 39-month period from 2013 to 2016 participated in the underlying trial. However, the analysis was restricted to patients who had colorectal surgery lasting at least 2 h. The amount of intraoperative inspired oxygen was randomly assigned for the initial 2 weeks, and then alternated every 2 weeks between 30% and 80%. No other aspects of ventilation were controlled, nor was postoperative FIO<sub>2</sub>. As a safety measure, clinicians were instructed to give enough oxygen to maintain oxygen saturation measured by pulse oximetry at or above 95%. During anesthetic induction and emergence, 100% inspired oxygen was allowed.

In the underlying trial, patients with missing oxygen data or baseline covariables and reoperations during the same hospitalization were excluded from analysis. We further restricted our primary analysis to patients with a home address in Ohio because we could obtain reliable vital status data from the Ohio Department of Health (Columbus, Ohio) for them. Ohio Death Index data are maintained by Ohio Department of Health and were updated to December 12, 2018, when we accessed the registry. Vital status and follow-up dates were identified using Cleveland Clinic Epic system and Ohio Death Index: (1) from the Epic system, we extracted patient death information and the latest office visit date; and (2) for patients with a home address in Ohio, we also determine their vital status from the Ohio Death Index. When death was not recorded in the Ohio index, statistical analyses were censored at the latest office visit date.

#### Statistical Methods

We descriptively compared the 80% and 30% oxygen patients based on demographic, baseline, and procedural variables using standard descriptive statistics and the absolute standardized difference. The absolute standardized difference was calculated as the absolute difference in means or proportions divided by the pooled SD, and any imbalanced factor with absolute standardized difference greater than 0.10 was adjusted for in the analyses.

We assessed the effect of 80% versus 30% target-inspired oxygen on long-term mortality using a Cox proportional hazards regression model incorporating patient as a random effect to account for correlation within some patients across multiple surgeries. Kaplan-Meier survival estimates were calculated. When patients were included more than once, previous surgeries were censored the day before the date of the subsequent surgery. Since some patients who participated several times received different treatments, we conducted sensitivity analyses by retaining only the first or last surgery or all surgeries to assess the robustness of our statistical methods. In the primary analysis, we used several methods to assess the proportional hazards assumption, including testing the interaction between treatment and log (time), a correlation test based on the weighted Schoenfeld residuals, a Supremum test, and a visual display of log (hazards) versus time.

We assessed heterogeneity of the treatment effect across levels of selected baseline variables using Cox proportional hazards regression and testing the treatment-by-variable interaction. Baseline factors of interest, assessed in separate models, included type of surgery (colorectal resection *vs.* others), age (less than 60 *vs.* greater than or equal to 60 yr), sex (female *vs.* male), American Society of Anesthesiologists (ASA; Schaumburg, Illinois) physical status (I to II *vs.* III to V), primary diagnosis (cancer *vs.* other), body mass index (less than 30 kg/m<sup>2</sup> *vs.* greater than or equal to 30 kg/m<sup>2</sup>), current smoking (yes *vs.* no), and laparoscopic surgery (yes *vs.* no). The treatment effect was assessed within levels of each factor.

As this study represents a *post hoc* analysis using available data from the original trial, we did not conduct an *a priori* power calculation. In a *post hoc* power calculation, we assumed that a hazard ratio of 1.2 or stronger was clinically important, indicating that patients in the treatment arm (or control group, since the test was two-tailed) had 20% higher chance of dying at any time during follow-up *versus* control. Using the estimated survival of 77% at 6 yr in our control group as reference, and assuming survival times followed an exponential distribution, with the attained sample size of 3,471, we could only detect a hazard ratio of 1.24 or stronger with 80% power.

Results are reported as hazard ratios. A two-sided significance level of 0.05 was used for the overall assessment. The significance criterion for each interaction was set to 0.05/8 = 0.0062. SAS 9.4 software (SAS Institute, USA) was used.

#### **Results**

The underlying trial was conducted at the Cleveland Clinic Main Campus from January 28, 2013, to March 11, 2016. The original trial analyzed 4,088 patients who had 5,167 surgeries and assessed the treatment effect on a 30-day composite of deep tissue or organ-space surgical site infection, healing-related wound complications, and mortality. For the primary analysis of this *post hoc* analysis, a total of 3,471 qualifying colorectal surgeries performed in 2,801 Ohio patients were analyzed, including 1,753 (51%) surgeries in 1,577 patients assigned to 80% oxygen and 1,718 surgeries in 1,551 patients qualifying for the current analysis, 457 were enrolled twice and 101 were enrolled three or more times; 327 patients received different treatments.

The 80% and 30% oxygen groups were well balanced on most of demographic, baseline, and procedural variables (absolute standardized difference less than 0.10, table 1) except smoking (absolute standardized difference, 0.110) and time-weighted average intraoperative heart rate (absolute standardized difference, 0.119). Overall mortality was 13.8% after a median (25th, 75th percentiles) follow-up period of 3.2 (0.5, 4.9) yr. We did not find an effect of 80% versus 30% oxygen on long-term mortality, with an estimated hazard ratio of 0.94 (95% CI, 0.78 to 1.13; P = 0.493; table 2, fig. 2). After 5 yr, the estimated survival rate was 80% (95% CI, 78 to 83%) in patients assigned to 80% oxygen and 80% (95% CI, 77 to 82%) in those assigned to 30% oxygen. For the primary analysis, Kaplan-Meier curves were close to each other and nonoverlapping. While the treatment-by-time interaction was significant (P = 0.019), the other two proportional hazards tests were not (correlation test based on the weighted Schoenfeld residuals, P = 0.202; and supremum test, P = 0.233). We thus concluded that there was no clinically meaningful violation of the proportional hazard assumption.



#### Table 1. Baseline and Procedural Variables for Ohio Patients (N = 3,471)

| Variables  | 80% Oxygen<br>(N = 1, 753) | 30% Oxygen<br>(N = 1, 718) | Absolute<br>Standardized<br>Difference* |
|--|----------------------------|----------------------------|---|
| Age, yr  | 54 ± 17                    | 53 ± 17                    | 0.038                                   |
| Sex, No. (%)                                       |                            |                            | 0.015                                   |
| Female   | 902 (51)                   | 897 (52)                   |   |
| Male   | 851 (49)                   | 821 (48)                   | 0.050                                   |
| Kace, No. (%)                                      | 1560 (90)                  | 1400 (07)                  | 0.056                                   |
| Black  | 1000 (09)                  | 1490 (07)                  |   |
| Other  | 30 (2)                     | 33 (2)                     |   |
| Body mass index, kg/m <sup>2</sup>                 | 26 [23, 31]                | 27 [23, 31]                | 0.015                                   |
| Smoking status, No. (%)                            |                            |                            | 0.110                                   |
| Current smoker                                     | 235 (13)                   | 170 (10)                   |   |
| Ex-smoker  | 517 (30)                   | 521 (30)                   |   |
| Never smoker                                       | 1001 (57)                  | 1027 (60)                  |   |
| ASA physical status, No. (%)                       | 0 (0)                      | = (0)                      | 0.007                                   |
|  | 8 (0)                      | 7 (0)                      |   |
|  | 517 (30)<br>1077 (61)      | 501 (29)                   |   |
|  | 1/0 (0)                    | 1/12 (02)                  |   |
| V  | 2 (0)                      | 0 (0)                      |   |
| Medical history No. (%)                            | 2 (0)                      | 0 (0)                      |   |
| Condestive heart failure                           | 71 (4)                     | 76 (4)                     | 0.019                                   |
| Vascular disease                                   | 69 (4)                     | 73 (4)                     | 0.016                                   |
| Pulmonary circulation disease                      | 85 (5)                     | 67 (4)                     | 0.046                                   |
| Peripheral vascular disease                        | 129 (7)                    | 111 (7)                    | 0.035                                   |
| Hypertension, uncomplicated                        | 618 (35)                   | 607 (35)                   | 0.002                                   |
| Hypertension, complicated                          | 83 (5)                     | 80 (5)                     | 0.004                                   |
| Paralysis  | 20 (1)                     | 16 (1)                     | 0.021                                   |
| Other neurologic disorders                         | 84 (5)                     | 106 (6)                    | 0.061                                   |
| Chronic pulmonary disease                          | 281 (16)                   | 266 (16)                   | 0.015                                   |
| Diabetes without chronic complications             | 176 (10)                   | 164 (10)                   | 0.017                                   |
| Diabeles with chronic complications                | 49 (3)<br>170 (10)         | 00 (4)<br>102 (11)         | 0.040                                   |
| Repat failure                                      | 98 (6)                     | 97 (6)                     | 0.031                                   |
| l iver disease                                     | 50 (0)                     | 53 (3)                     | 0.002                                   |
| Peptic ulcer disease (bleeding)                    | 2 (0)                      | 1 (0)                      | 0.019                                   |
| AIDS   | 3 (0)                      | 1 (0)                      | 0.033                                   |
| Lymphoma   | 37 (2)                     | 35 (2)                     | 0.005                                   |
| Metastatic cancer                                  | 147 (8)                    | 161 (9)                    | 0.035                                   |
| Solid tumor without metastasis                     | 381 (22)                   | 311 (18)                   | 0.091                                   |
| Rheumatoid arthritis/collagen vascular disease     | 85 (5)                     | 84 (5)                     | 0.002                                   |
| Coagulopathy                                       | 144 (8)                    | 124 (7)                    | 0.037                                   |
| UDESITY<br>Weight Loop                             | 383 (22)                   | 421 (25)                   | 0.063                                   |
| Fluid and electrolyte disorders                    | 525 (50)<br>815 (47)       | 512 (50)<br>798 (46)       | 0.001                                   |
| Chronic blood loss anemia                          | 57 (3)                     | 56 (3)                     | 0.001                                   |
| Deficiency anemias                                 | 432 (25)                   | 450 (25)                   | 0.036                                   |
| Alcohol abuse                                      | 37 (2)                     | 35 (2)                     | 0.005                                   |
| Drug abuse   | 54 (3)                     | 55 (3)                     | 0.007                                   |
| Psychoses  | 108 (6)                    | 99 (6)                     | 0.017                                   |
| Depression   | 343 (19)                   | 318 (19)                   | 0.027                                   |
| Primary diagnosis, No. (%)                         |                            |                            | 0.062                                   |
| Cancer   | 833 (48)                   | 788 (46)                   |   |
| Uronn disease                                      | 280 (16)                   | 280 (16)                   |   |
|  | 168 (10)                   | 169 (10)                   |   |
| USIUIIIY<br>Fictula                                | 135 (8)<br>115 (6)         | 127 (7)<br>131 (9)         |   |
| Hernia   | (0)<br><u>41</u> (2)       | ΔΔ (3)                     |   |
| Other  | 181 (10)                   | 179 (10)                   |   |
| Preoperative oral antibiotic, No. (%)              | 811 (46)                   | 804 (47)                   | 0.011                                   |
| Preoperative bowel preparation medication, No. (%) | 376 (21)                   | 343 (20)                   | 0.037                                   |
| Type of surgery, No. (%)                           | . ,                        | . *                        | 0.074                                   |
|  |                            |                            | (Continued)                             |

#### Table 1. (Continued)

|   |                    |                   | Absolute     |
|---|--------------------|-------------------|--------------|
|   | 80% Oxygen         | 30% Oxygen        | Standardized |
| Variables   | (N = 1, 753)       | (N = 1, 718)      | Difference*  |
|   |                    |                   |              |
| Colorectal resection  | 951 (54)           | 896 (52)          |              |
| Lower gastrointestinal therapeutic procedures                     | 523 (30)           | 525 (31)          |              |
| Small bowel resection   | 99 (6)             | 104 (6)           |              |
| Exploratory laparotomy  | 35 (2)             | 48 (3)            |              |
| Excision  | 30 (2)             | 29 (2)            |              |
| Laparoscopy   | 35 (2)             | 36 (2)            |              |
| Hernia repair   | 39 (2)             | 39 (2)            |              |
| leostomy and other enterotomy                                     | 21 (1)             | 26 (1)            |              |
| Colostomy   | 20 (1)             | 15 (1)            |              |
| Laparoscopic surgery (vs. open or converted), No. (%)             | 508 (29)           | 469 (27)          | 0.037        |
| Duration of surgery, h  | 4.2 ± 1.7          | 4.2 ± 1.8         | 0.030        |
| Regional block, No. (%)   | 42 (2)             | 59 (3)            | 0.062        |
| Spinal or epidural anesthesia, No. (%)                            | 133 (8)            | 144 (8)           | 0.029        |
| Attending anesthesiologist,‡ No. (%)                              |                    |                   | —†           |
| A   | 231 (13)           | 228 (13)          |              |
| В   | 241 (14)           | 223 (13)          |              |
| C   | 73 (4)             | 101 (6)           |              |
| D   | 82 (5)             | 51 (3)            |              |
| E   | 39 (2)             | 58 (3)            |              |
| Operating room number, No. (%)                                    |                    |                   | 0.076        |
| #47   | 388 (22)           | 357 (21)          |              |
| #48   | 371 (21)           | 348 (20)          |              |
| #50   | 310 (18)           | 320 (19)          |              |
| #46   | 259 (15)           | 253 (15)          |              |
| #45   | 256 (15)           | 265 (15)          |              |
| #49   | 93 (5)             | 112 (6)           |              |
| #40–44  | 76 (4)             | 63 (4)            |              |
| Intraoperative management   |                    |                   |              |
| Time-weighted average of esophageal                               |                    |                   |              |
| temperature, °C   | $36.0 \pm 0.6$ §   | $36.0 \pm 0.6$    | 0.061        |
| Esophageal temperature at end of case, °C                         | 36.4 [35.9, 36.8]§ | 36.4 [35.9, 36.8] | 0.007        |
| Time-weighted average of MAP, mmHg                                | 86 ± 9             | 85 ± 9            | 0.096        |
| Time-weighted average of HR, beats/min                            | 76 ± 11            | 78 ± 12           | 0.119        |
| Amount of anesthetic gas (MAC), h                                 | 2.9 [2.0, 4.2]#    | 2.9 [2.0, 4.1]**  | 0.019        |
| Fraction of inspired oxygen, %                                    | 80 [78, 82]        | 39 [35, 47]       | 3.121        |
| Time-weighted average of PETCO,, mmHg                             | 35 ± 2             | $35 \pm 2$        | 0.033        |
| Time-weighted average of glucose, mg/dl                           | 141 [121, 164]††   | 140 [118, 164]‡‡  | 0.053        |
| Crystalloid volume, I   | 2.7 [2, 3.5]       | 2.8 [2, 3.6]      | 0.028        |
| Laparoscopic surgery  | 2.8 [2.2, 3.4]     | 2.8 [2.2, 3.5]    |              |
| Open surgery  | 2.6 [1.8, 3.6]     | 2.7 [1.8, 3.6]    |              |
| Colloid volume, I   | 0 [0, 0.25]        | 0 [0, 0.5]        | 0.094        |
| Estimated blood loss, ml  | 100 [50, 200]      | 100 [50, 250]     | 0.050        |
| Blood transfusion, No. (%)  | 142 (8)            | 144 (8)           | 0.010        |
| Amount of blood transfusion among patients who were transfused, I | 0.7 [0.4, 1.0]     | 0.7 [0.4, 1.0]    | 0.012        |

Summary statistics (presented as percentage of patients, mean ± SD, or median [25th, 75th percentiles] for factors, symmetric continuous variables, and skewed continuous variables, respectively).

\*Absolute standardized difference: absolute difference in means or proportions divided by the pooled SD. Any baseline or procedural variables with an absolute standardized difference greater than 0.10 was considered to be imbalanced and would be adjusted for in the analysis. †Absolute standardized difference was not calculated due to too many categories (among 64 anesthesiologists). ‡Five attending anesthesiologists (of 64) are listed due to the limited space. §A total of 80 cases have missing data. ||A total of 58 patients have missing data. #Two cases have missing data. \*Five cases have missing data. †A total of 1,239 cases have missing data. ‡A total of 1,178 cases have missing data.

AIDS, acquired immune deficiency syndrome; ASA, American Society of Anesthesiologists; HR, heart rate; MAC, minimal alveolar concentration; MAP, mean arterial blood pressure; PETCO<sub>2</sub>, end-tidal pressure of carbon dioxide.

There were also no differences in the relative effects of oxygen in cancer and noncancer patients (fig. 3). The effect of oxygen on mortality also did not depend on the type of surgery, age, body mass index, smoking status, ASA physical status, primary diagnosis, or surgical approach (fig. 3). Results were similar when the analysis was restricted to only the first or last surgery or including patients from all states (appendix table A1). Demographic, baseline, and procedural variables are shown in appendix table A2 for the first surgery of Ohio patients, and in appendix table A3 for the last surgery of Ohio patients. Table 2. Primary Results: Effect of 80% versus 30% Oxygen Supplement on Long-term mortality in Ohio Patients (N = 3,471 Surgeries)

|  | N     | Long-term<br>Mortality (%) | Median<br>Follow-up (yr) [25th,<br>75th Percentiles] | 2-yr<br>Survival %<br>(95% Cl) | 5-yr<br>Survival %<br>(95% Cl) | Hazard<br>Ratio<br>(95% Cl) | <i>P</i><br>Value |
|--|-------|----------------------------|--|--------------------------------|--------------------------------|-----------------------------|-------------------|
| Primary analysis (all operations)*     |       |                            |  |                                |                                |                             | 0.493             |
| 30% Oxygen                             | 1,718 | 245 (14)                   | 3.1 [0.5, 4.9]                                       | 90% (88–92%)                   | 80% (77–82%)                   | Reference = 1               |                   |
| 80% Oxygen                             | 1,753 | 234 (13)                   | 3.2 [0.5, 4.9]                                       | 91% (89–92%)                   | 80% (78–83%)                   | 0.94 (0.78–1.13)            |                   |
| Sensitivity analyses                   |       |                            |  | . ,                            | . ,                            | · · · ·                     |                   |
| Only the first operation per patient † |       |                            |  |                                |                                |                             | 0.615             |
| 30% Oxygen                             | 1,391 | 244 (18)                   | 4.1 [1.7, 5.4]                                       | 90% (88–92%)                   | 80% (77–82%)                   | Reference = 1               |                   |
| 80% Oxygen                             | 1,410 | 235 (17)                   | 4.1 [1.6, 5.4]                                       | 90% (88–92%)                   | 80% (78–83%)                   | 0.95 (0.80-1.14)            |                   |
| Only the last operation per patient ‡  |       |                            |  |                                |                                |                             | 0.681             |
| 30% Oxygen                             | 1,389 | 245 (18)                   | 4.0 [1.5, 5.2]                                       | 89% (88–91%)                   | 79% (77–82%)                   | Reference = 1               |                   |
| 80% Oxygen                             | 1,412 | 234 (17)                   | 4.0 [1.4, 5.2]                                       | 90% (88–91%)                   | 80% (77–82%)                   | 0.96 (0.80-1.15)            |                   |

\*Multivariable random-effects Cox proportional hazards regression adjusting for smoking status and time-weighted average of intraoperative heart (*i.e.*, imbalanced with absolute standardized difference greater than 0.1 in table 1), and incorporating cluster-specific random effects of multiple surgeries within patients. †Multivariable random-effects Cox proportional hazards regression adjusting for smoking status, time-weighted average of intraoperative mean arterial pressure (*i.e.*, imbalanced with absolute standardized difference greater than 0.1 in table A2). ‡Multivariable random-effects Cox proportional hazards regression adjusting for time-weighted average of intraoperative mean arterial pressure (*i.e.*, imbalanced with absolute standardized difference greater than 0.1 in table A2). ‡Multivariable random-effects Cox proportional hazards regression adjusting for time-weighted average of intraoperative heart rate, smoking status, and intraoperative colloids infusion (*i.e.*, imbalanced with absolute standardized difference greater than 0.1 in table A3).

#### **Discussion**

We conducted a *post hoc* analysis of a single-center crossover cluster trial. The original trial tested the hypothesis that supplemental oxygen decreases the incidence of postoperative wound infections and infection-related complications.<sup>12</sup> The use of a novel crossover cluster design allowed rapid enrollment of approximately 5,100 surgeries on 4,088 patients. As might be expected for a subset with about 2,800 patients who had more than 3,400 operations, there was remarkably good balance between the groups on a long list of observed

potential confounding factors. Long-term mortality hazard was nearly identical in patients assigned to 30% and 80% intraoperative oxygen. Our results are therefore inconsistent with the theory that high intraoperative inspired oxygen promotes long-term mortality after colorectal surgery.

Our findings are consistent with those of Podolyak *et al.*, who analyzed long-term mortality in more than 900 patients who participated in various randomized trials conducted more than a decade ago.<sup>21</sup> Supplemental oxygen did not increase long-term mortality, with an overall site-stratified



**Fig. 2.** Kaplan–Meier survival curve estimates comparing patients assigned to receive 80% and 30% intraoperative inspired oxygen. The hazard ratio was an estimated 0.94 (95% CI, 0.78 to 1.13; P = 0.493).



**Fig. 3.** Hazard ratios of the primary outcome of long-term mortality in patients assigned to 80% *versus* 30% oxygen within the levels of the selected factors. The significance criterion for each interaction was set to 0.05/8 = 0.0062, and the significance criterion was 0.0031 for each comparison (*i.e.*, 0.05 of 16), and thus 99.6% Cls are plotted. None of the interactions between the treatment and these factors was statistically significant on the primary outcome (all P > 0.0062).

hazard ratio of 0.93 (95% CI, 0.72 to 1.20).<sup>21</sup> Our current results and those of Podolyak *et al.*<sup>21</sup> contrast with those reported by the PROXI investigators, who randomized 1,400 patients to 30% or 80% inspired intraoperative oxygen. The primary outcome was surgical site infection, which did not differ. In a secondary analysis, mortality was substantially increased in patients given supplemental intraoperative oxygen (hazard ratio, 1.31 [95% CI, 1.03 to 1.66]).<sup>14</sup>

Why the PROXI results are discrepant remains unclear. Mortality in the PROXI trial was evaluated over a median of 2.3 yr *versus* 4.7 yr in our current analysis, and a range between 3.6 and 13.6 yr in the analysis of Podolyak *et al*. However, longer follow-up periods in the more recent articles<sup>21</sup> do not explain reported mortality differences since the hazard ratios were similar throughout the follow-up periods. There were substantive differences among the three analyses in terms of patient age, the fractions of laparoscopic and emergency procedures, and the types of procedures. However, subgroup analyses in our current study showed no significant interaction with type of surgery, age, body mass index, smoking, ASA physical status, or surgical approach. It therefore seems unlikely that any of these factors greatly influences the relative effect of inspired oxygen concentration on long-term mortality or explains why mortality differed with oxygen concentration in PROXI but not in subsequent reports.

In the PROXI trial, supplemental oxygen increased longterm mortality specifically in a subgroup of 352 cancer patients. The investigators proposed that high  $Fio_2$  increased long-term mortality in cancer patients by promoting the growth of circulating tumor cells after potentially curative surgery. In a subsequent substudy of the PROXI trial, however, the authors could not demonstrate that 80% oxygen increases the incidence of new cancer or cancer recurrence. Although new or recurrent cancers occurred 100 days earlier in patients receiving supplemental oxygen, earlier recurrence was insufficient to explain the excess mortality in cancer patients.<sup>20</sup> In our study, 80% inspired oxygen did not augment long-term mortality in 995 cancer patients, nor did it in 451 cancer patients in the study by Podolyak *et al.*<sup>21</sup> Data from 1,446 patients, therefore, do not

support the theory that supplemental oxygen has long-term toxicity specific to cancer surgical patients.

We used the Ohio Death Index from the Ohio Department of Health to evaluate mortality. The Ohio Death Index has high validity for vital status.<sup>25</sup> However, 31% of patients in the underlying trial lived elsewhere. The analysis population was thus restricted to 2,801 patients. Nonetheless, we report by far the largest trial of inspired intraoperative oxygen and mortality.

A partial limitation of our analysis is that approximately 20% of patients had more than one operation. For these patients, previous surgeries were censored the day before the date of the next surgery since some of them might receive different treatments. We adjusted for the potential within-patient correlation by including patient as a random effect. An advantage of retaining all cases during the study period is that we gained power and perhaps generalizability. However, we also conducted sensitivity analyses restricted to the first or last surgery; the results were similar, indicating that our statistical methods were robust. An additional limitation is that the inspired oxygen concentration in patients assigned to receive 30% was actually given with a median of 39% [Q1, Q3: 35%, 47%]. However, the higher concentration was not a protocol deviation because clinicians were instructed to give sufficient oxygen to maintain an oxygen saturation of at least 95%. Many of our patients needed more oxygen because they were obese and/or required Trendelenburg positioning, which decreased their saturation.

We assumed that a hazard ratio less than or equal to 0.83 or greater than or equal to 1.2 was clinically important. The 95% CI of the hazard ratio for the primary analysis was within 0.78 and 1.13, which was fairly narrow, and the upper limit of 1.13 was not beyond what the study was designed to detect (a hazard ratio of 1.2 or more). Therefore, it allows us to make a fairly strong negative conclusion.

In summary, we performed a *post hoc* analysis of a large crossover cluster trial and evaluated whether intraoperative supplemental oxygen causes long-term mortality. Supplemental oxygen did not increase postoperative mortality overall, or in cancer patients, and can be safely used when deemed appropriate.

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Support was provided solely from institutional and/or departmental sources.

#### **Competing Interests**

The authors declare no competing interests.

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# Appendix

**Table A1.** Sensitivity Analyses: Effect of 80% *versus* 30% Oxygen Supplement on Long-term Mortality Including Patients from All States (N = 5,167)

|                                       | N     | Long-term<br>Mortality (%) | Median Follow-up<br>(yr) [25th,<br>75th Percentiles] | 2-yr<br>Survival %<br>(95% Cl) | 5-yr<br>Survival %<br>(95% CI) | Hazard Ratio<br>(95% CI) | <i>P</i><br>Value |
|---------------------------------------|-------|----------------------------|--|--------------------------------|--------------------------------|--------------------------|-------------------|
| All operations*                       |       |                            |  |                                |                                |                          | 0.534             |
| 30% Oxygen                            | 2,552 | 267 (10)                   | 1.7 [0.4, 4.5]                                       | 92% (90–93%)                   | 82% (80-84%)                   | Reference = 1            |                   |
| 80% Oxygen                            | 2,615 | 257 (10)                   | 1.6 [0.3, 4.5]                                       | 92% (91-93%)                   | 83% (80-85%)                   | 0.95 (0.80-1.13)         |                   |
| Only the first operation per patient† |       |                            |  |                                |                                |                          | 0.656             |
| 30% Oxygen                            | 2,040 | 268 (13)                   | 3.4 [0.8, 5.1]                                       | 92% (90–93%)                   | 82% (80-84%)                   | Reference = 1            |                   |
| 80% Oxygen                            | 2,048 | 256 (13)                   | 3.4 [0.7, 5.1]                                       | 91% (90–93%)                   | 83% (80-85%)                   | 0.96 (0.81-1.14)         |                   |
| Only the last operation per patient‡  |       |                            |  |                                |                                |                          | 0.548             |
| 30% Oxygen                            | 2,011 | 267 (13)                   | 3.3 [0.7, 4.9]                                       | 91% (90–92%)                   | 81% (79–84%)                   | Reference = 1            |                   |
| 80% Oxygen                            | 2,077 | 257 (12)                   | 3.3 [0.5, 4.9]                                       | 91% (90–92%)                   | 82% (79–84%)                   | 0.95 (0.80–1.13)         |                   |

\*Multivariable random-effects Cox proportional hazards regression adjusting for time-weighted average of intraoperative heart rate (*i.e.*, imbalanced with absolute standardized difference greater than 0.1) and incorporating cluster-specific random effects of multiple surgeries within patients. †Multivariable random-effects Cox proportional hazards regression adjusting for smoking status (*i.e.*, imbalanced with absolute standardized difference greater than 0.1). ‡Multivariable random-effects Cox proportional hazards regression adjusting for time-weighted average of intraoperative heart rate (*i.e.*, imbalanced with absolute standardized difference greater than 0.1).

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| $\begin{array}{c c c c c c c c c c c c c c c c c c c $  | Variables   | 80% Oxygen<br>(N = 1, 410) | 30% Oxygen<br>(N = 1, 391) | Absolute<br>Standardized<br>Difference* |
|---|---|----------------------------|----------------------------|---|
| Gender, hor, (b)0.2280.2380.238MaleR52 (49)736 (5.3)748 (5.4)MaleR52 (48)853 (47)0.64White1224 (89)1208 (87)0.64White123 (10)223 (2.3)727 (2.3.   | Age, yr   | 55 ± 17                    | 55 ± 17                    | 0.028                                   |
| Fendle     728 (52)     738 (5)       Made     652 (43)     655 (47)       Race, Nc (%)     0.64       White     1238 (87)     1208 (87)       Black     133 (10)     155 (1)       Other     23 (1)     22 (2, 32)     0.000       Sex, Nx (%)     0.153     0.000       Current anoker     137 (14)     128 (9)     0.153       Current anoker     137 (14)     128 (9)     0.000       Never anoker     728 (55)     356 (60)     0.001       Never anoker     151 (30)     381 (27)     0.001       I     6 (6)     7 (0)     0.011       X     2 (8)     133 (10)     1001       V     2 (8)     133 (10)     1011       V     2 (8)     133 (10)     1011       <   | Gender, No. (%)                                   |                            |                            | 0.026                                   |
| Mele     682 (48)     653 (48)     0.064       White     1254 (89)     1284 (87)     0       Black     133 (10)     155 (11)     0       Other     223 (1)     282 (2)     0.030       Smaking stuss, No. (%)     72 [23, 31]     27 [23, 32]     0.030       Current smoker     197 (14)     128 (9)     0.030       Never smoker     742 (25)     836 (60)     0       Never smoker     760 (9)     7 (0)     1       I     6 (0)     7 (0)     1     0.040       V     2 (9)     131 (10)     27 (14)     0.027       V     128 (9)     131 (10)     27 (14)     0.027       V     2 (9)     131 (10)     27 (14)     0.027       Valuancer scituation disease     57 (14)     64 (5)     0.027       Valuancer scituation disease     59 (7)     33 (6)     0.040       Hypertension, complication     51 (1)     15 (1)     0.017       Periptient vascular disease     58 (7)     33 (3)     0.017  | Female  | 728 (52)                   | 736 (53)                   |   |
| Race, No, No,     Under     1224 (49)     1208 (47)       Bick,     133 (10)     155 (11)       Other     23 (2)     21 (23, 31)     22 (23, 32)     0.030       Smoking status, No, (%)     0.153     0.153     0.153     0.153       Current snoker     137 (14)     128 (9)     0.153       Sack physical status, No, (%)     0.153     0.000     0.001       Never snoker     6 (0)     7 (0)     0.001       ASA physical status, No, (%)     0.001     0.001     0.001       V     6 (0)     7 (0)     0.001       V     22 (8)     133 (10)     V       Medical history, No, (%)     0.001     0.001       V     120 (8)     133 (10)     0.015       Puriforal Vaccutar disease     69 (6)     52 (4)     0.057       Paripheral Vaccutar disease     69 (7)     38 (6)     0.011       Puriforal Vaccutar disease     69 (7)     38 (6)     0.015       Puriforal Vaccutar disease     69 (3)     0.015     0.015       Purotheral Vaccutar di   | Male  | 682 (48)                   | 655 (47)                   |   |
| Mine     1254 (89)     1234 (8)       Black     123 (1)     155 (1)       Other     23 (1)     24 (2)       Body mass index, kym²     27 [23, 31]     27 [23, 31]     0.030       Smoking stuss, No, (%)     7 [23, 31]     27 [23, 31]     0.030       Current smoker     197 (14)     128 (9)     0.040       R-x moker     72 [23, 31]     47 (23, 31)     47 (23, 31)       Newer smoker     72 (25)     836 (60)     0.040       I     6 (0)     7 (0)     1       I     6 (0)     7 (0)     1       II     415 (30)     381 (27)     1       V     2 (0)     0 (0)     0     1       Valid story, No, (%)     2 (0)     0 (0)     0     0       Valid story, No, (%)     2 (0)     6 (1)     0.017     1       Valid story, No, (%)     2 (0)     15 (1)     0.017     1       Valid story, No, (%)     2 (0)     15 (1)     0.017     1       Valid stor disease     9 (6)     5 (2) (4) <td>Race, No. (%)</td> <td></td> <td></td> <td>0.064</td>   | Race, No. (%)                                     |                            |                            | 0.064                                   |
| Black     133 (10)     153 (1)     28 (2)       Other     23 (1)     28 (2)     0.030       Body mass index, kg/m²     157     0.153       Current annoker     197 (14)     28 (9)     153       Current annoker     782 (55)     836 (80)     0.400       Never annoker     782 (55)     836 (80)     0.400       I     6 (0)     7 (0)     1       I     6 (0)     7 (0)     1       III     6 (5)     57 (4)     6 (4 (5)     0.027       V     2 (0)     0 (0)     1     0.057       V vascular disease     55 (61)     57 (4)     64 (5)     0.027       Pulmonary circulation disease     66 (5)     52 (4)     0.057       Vascular disease     56 (5)     52 (4)     0.057       Pulmetary sizz diret disease     68 (5)     52 (4)     0.017       Paripheral vascular disease     68 (5)     52 (4)     0.017       Paripheral vascular disease     15 (1)     15 (1)     0.013       Uher denologic disorders  | White   | 1254 (89)                  | 1208 (87)                  |   |
| Other     23 (1)     27 (23, 31)     27 (23, 32)     0.030       Smoking status, No. (%)     0.153     0.153       Current smoker     197 (14)     128 (9)     0.153       Neer smoker     782 (55)     386 (60)     0.040       Neer smoker     782 (55)     383 (60)     0.040       I     6.00     7.00     0.040       I     6.00     7.00     0.040       I     6.00     7.00     0.000       I     6.00     7.00     0.00       V     2.00     0.00     0.00       V     2.00     0.00     0.00       V     2.00     0.00     0.007       Vascular disease     57 (4)     64 (5)     0.027       Vascular disease     9.97     8.3 (6)     0.040       Hypertansion, complicated     507 (38)     40 (55)     0.015       Hypertansion, complications     15 (1)     15 (1)     0.015       Hypertansion, complications     16 (4)     81 (6)     0.017       Dishetes Mitho  | Black   | 133 (10)                   | 155 (11)                   |   |
| Body mass index, Kg/m <sup>2</sup> 27 (23, 31)     27 (23, 32)     0.030       Distance and the set of the set o  | Other   | 23 (1)                     | 28 (2)                     |   |
| Smoking status, No. (%)     0.153       Current smoker     197 (14)     128 (9)       Rever smoker     782 (55)     836 (0)       ASA physical status, No. (%)     0.040       I     65 (0)     70 (0)       II     65 (0)     70 (0)       II     65 (0)     70 (6)       V     128 (9)     133 (10)       V     2 (0)     0.00       Vascudar disease     57 (4)     64 (5)     0.027       Vascudar disease     98 (7)     83 (6)     0.040       Hypertansion, complicated     57 (4)     64 (6)     0.017       Parkings     15 (1)     15 (1)     001     001       Distates without chronic complications     145 (10)     136 (10)     0.017       Distates without chronic complications <t< td=""><td>Body mass index, kg/m<sup>2</sup></td><td>27 [23, 31]</td><td>27 [23, 32]</td><td>0.030</td></t<>   | Body mass index, kg/m <sup>2</sup>                | 27 [23, 31]                | 27 [23, 32]                | 0.030                                   |
| Lurrent strucker     19' (14)     128 (9)       Ex-smoker     782 (5)     363 (60)       ASA physical status, No. (%)     0.040       I     6 (0)     7 (0)       II     6 (0)     7 (0)       III     859 (61)     381 (27)       III     859 (61)     570 (63)       V     2 (0)     0.00       V     2 (0)     0.027       Vascular disease     57 (4)     64 (5)     0.027       Purimonary circulation disease     57 (3)     480 (5)     0.017       Purimonary circulation disease     69 (7)     52 (4)     0.057       Purimonary circulation disease     69 (7)     53 (6)     0.015       Hypertension, complication     507 (36)     480 (35)     0.015       Hypertension, complication     15 (1)     15 (1)     0.011       Other neurologic disorders     61 (4)     81 (6)     0.068       Chrance pulmonary disease     39 (3)     39 (3)     0.012       Diabetes without chronic complications     145 (10)     136 (10)     0.013 <tr< td=""><td>Smoking status, No. (%)</td><td></td><td>4.00 (0)</td><td>0.153</td></tr<>  | Smoking status, No. (%)                           |                            | 4.00 (0)                   | 0.153                                   |
| Lessmoder     431 (31)     427 (30)       ASA physical status, No. (%)     0.040       I     6 (0)     7 (0)       II     415 (30)     351 (27)       II     6 (0)     7 (0)       II     415 (30)     870 (63)       V     128 (9)     133 (10)       V     2 (0)     0 (0)       Medical history, No. (%)     7 (4)     64 (5)     0.027       Vascular disease     69 (5)     52 (4)     0.045       Peripheral scalar disease     69 (5)     52 (4)     0.047       Paramary circulation disease     69 (5)     52 (4)     0.047       Propriperal scalar disease     69 (5)     52 (4)     0.047       Paraphasi     57 (4)     64 (5)     0.027       Parabasi     57 (4)     64 (5)     0.027       Parabasi     57 (4)     64 (5)     0.017       Parabasi     507 (35)     490 (35)     0.017       Parabasi     16 (4)     16 (6)     0.058       Chronic pulmonary disease     28 (2)     24   | Current smoker                                    | 197 (14)                   | 128 (9)                    |   |
| Never smoker     A26 (b):     C040       I     6 (0)     7 (0)       II     4 15 (30)     381 (27)       III     650 (61)     570 (63)       V     250 (9)     133 (10)       V     200 (00)     00       V     200 (00)     000       V     V     000 (00)     000       V     V     000 (00)     000 (00)       V     V     000 (00)     000 (00)       Vascidar disease     60 (0)     52 (4)     0.057       Paripheral vascidar disease     60 (0)     52 (4)     0.051       Hypertension, complicated     57 (4)     46 (5)     0.017       Paralysis     15 (1)     15 (1)     0.011       Ottoric primeray disease     61 (4)     16 (6)     0.062       Cornaci primeray disease     33 (2)     46 (5)     0.022 </td <td>Ex-smoker</td> <td>431 (31)</td> <td>427 (30)</td> <td></td>  | Ex-smoker   | 431 (31)                   | 427 (30)                   |   |
| ASA Brightal status, No. (%)     0.40     7.0       II     415 (30)     381 (27)       III     415 (30)     870 (63)       IV     128 (9)     133 (10)       V     128 (9)     133 (10)       Congestive heart failure     57 (4)     64 (5)     0.027       Vacular disease     57 (4)     64 (5)     0.027       Vacular disease     69 (5)     52 (4)     0.057       Peripheral vaccular disease     98 (7)     83 (6)     0.040       Hypertension, complicated     50 (36)     460 (5)     0.017       Paralysis     15 (1)     15 (1)     0.001       Other neurologic disorders     61 (4)     81 (6)     0.017       Paralysis     15 (1)     15 (1)     0.016       Other neurologic disorders     61 (4)     81 (6)     0.017       Diabetes with chronic complications     33 (2)     24 (15)     0.018       Diabetes with chronic complications     32 (2)     29 (2)     0.017       Diabetes with chronic complications     32 (2)     29 (2)     0.033   | Never smoker                                      | 782 (55)                   | 836 (60)                   | 0.040                                   |
| 1     0.00     7.00       II     415 (50)     337 (27)       III     859 (61)     870 (63)       IV     2.00     0.00       Welcal history, No. (%)     2.00     0.00       Congestive heart failure     57 (4)     64 (5)     0.027       Vascular disease     57 (4)     64 (5)     0.027       Putmonary circulation disease     69 (5)     52 (4)     0.057       Putmonary circulation disease     90 (7)     83 (6)     0.040       Hypertension, nucomplicated     57 (4)     64 (5)     0.017       Paralysis     15 (1)     15 (1)     0.001       Hypertension, nucomplicated     62 (4)     66 (5)     0.017       Paralysis     15 (1)     15 (1)     0.001     0.001       Other neurologic disorders     61 (4)     81 (6)     0.068       Chronic pulmonary disease     12 (10)     15 (11)     0.013       Diabetes with chronic complications     13 (2 (10)     15 (11)     0.033       Hypothyroidism     12 (0)     100     0.021   | ASA physical status, No. (%)                      | C (0)                      | 7 (0)                      | 0.040                                   |
| III     12 (40)     351 (27)       III     559 (61)     870 (63)       IV     128 (9)     133 (10)       V     20 (9)     00       Medical history, No. (%)     20 (9)     00       Congestive heat failure     57 (4)     64 (5)     0.027       Pascular disease     69 (5)     52 (4)     0.057       Peripheral vascular disease     69 (5)     52 (4)     0.057       Peripheral vascular disease     69 (5)     52 (4)     0.057       Peripheral vascular disease     69 (6)     490 (35)     0.015       Hypertension, uncomplicated     507 (65)     490 (35)     0.015       Other neurologic disorders     16 (4)     81 (6)     0.018       Diabetes with chronic complications     13 (2)     46 (3)     0.033       Benal faiture     74 (5)     77 (6)     0.013       Lure disease (heding)     29 (2)     29 (2)     0.002       Verpticur disease (heding)     29 (3)     30 (3)     0.002       Verpticur disease (heding)     29 (2)     29 (2)     0.002 <td></td> <td>6 (U)</td> <td>(U) 7</td> <td></td>   |   | 6 (U)                      | (U) 7                      |   |
| m     Congestive heat failure     2 (0)     0 (0)       V     2 (0)     0 (0)       Wedical history, No. (%)     2 (0)     0 (0)       Congestive heat failure     57 (4)     64 (5)     0.027       Vascular disease     69 (5)     52 (4)     0.057       Peripheral vascular disease     69 (5)     52 (4)     0.057       Paralysis     15 (1)     15 (1)     0.011       Paralysis     15 (1)     0.011     0.017       Diabetes without chronic complications     145 (10)     136 (10)     0.017       Diabetes without chronic complications     135 (10)     0.017     0.033       Diabetes without chronic complications     136 (10)     0.017     0.031       Liver disease     12 (0)     1 (0)     0.021     4.03 (0)     0.002       Mitoritre disease     2 (0)     1 (0) <td></td> <td>415 (30)</td> <td>381 (27)</td> <td></td>   |   | 415 (30)                   | 381 (27)                   |   |
| N     12 (9)     135 (10)       Medical history, No, (%)     2 (0)     0 (0)       Congestive heart failure     57 (4)     64 (5)     0.027       Vascular disease     59 (5)     52 (4)     0.057       Peripheral vascular disease     69 (5)     52 (4)     0.057       Peripheral vascular disease     98 (7)     83 (6)     0.040       Hypertension, uncomplicated     62 (4)     66 (5)     0.017       Paralysis     15 (1)     15 (1)     0.016       Other neurologic disorders     61 (4)     81 (6)     0.068       Chronic pulmorary disease     216 (15)     204 (15)     0.017       Diabetes with chronic complications     13 (2)     46 (3)     0.058       Hypothyroidism     142 (10)     154 (11)     0.033       Hypothyroidism     33 (2)     46 (3)     0.002       Albases     39 (3)     39 (3)     0.002       Mitter     74 (5)     77 (6)     0.013       Luer disease (bleading)     20 (1)     10 (0)     0.021       Albas     90 (7  |   | 859 (61)                   | 870 (03)                   |   |
| Value     2.00     0.00       Medical history, No. (%)     0.027       Congestive heart failure     57 (4)     64 (5)     0.027       Purinonary circulation disease     57 (4)     64 (5)     0.027       Purinonary circulation disease     69 (5)     52 (4)     0.057       Peripheral vascular disease     98 (7)     83 (6)     0.040       Hypertension, complicated     507 (35)     490 (35)     0.015       Hypertension, complicated     62 (4)     66 (5)     0.017       Paralysis     15 (1)     15 (1)     0.001       Other neurologic disorders     61 (4)     81 (6)     0.068       Chronic pulmonary disease     216 (15)     204 (15)     0.018       Diabetes without chronic complications     145 (10)     136 (10)     0.017       Diabetes without chronic complications     142 (10)     154 (11)     0.033       Renal failure     74 (5)     77 (6)     0.013       Liver disease (bleeding)     29 (2)     29 (2)     0.002       ADS     30 (0)     100     0.037     1  | IV<br>V   | 128 (9)                    | 133 (10)                   |   |
| metade instary  | V<br>Modical history No. (%)                      | 2 (0)                      | 0 (0)                      |   |
| Dougstor free frame     37 (4)     64 (5)     0.227       Pulmonary circulation disease     59 (5)     52 (4)     0.057       Peripheral vascular disease     98 (7)     83 (6)     0.040       Hypertension, complicated     507 (36)     490 (35)     0.015       Hypertension, complicated     51 (1)     15 (1)     0.001       Other neurologic disorders     61 (4)     81 (6)     0.008       Chronic pulmonary disease     216 (15)     224 (15)     0.018       Diabetes without chronic complications     145 (10)     156 (1)     0.033       Renal failure     74 (5)     77 (6)     0.033       Hypothyroidism     142 (10)     154 (11)     0.033       Renal failure     74 (5)     77 (6)     0.033       Liver disease     99 (3)     39 (3)     0.002       Petic ulcer disease (bleeding)     2 (0)     1 (0)     0.037       Liver disease     39 (3)     30 (3)     0.017       Solid tumour without metastasis     321 (23)     272 (20)     0.002       Metastatic cancer     39 (3) <td>Condective beart failure</td> <td>57 (1)</td> <td>64 (5)</td> <td>0.027</td>  | Condective beart failure                          | 57 (1)                     | 64 (5)                     | 0.027                                   |
| Pullinovary (cruciation disease)     51 (4)     0.167       Peripheral vascular disease     69 (5)     52 (4)     0.057       Peripheral vascular disease     59 (7)     83 (6)     0.400       Hypertension, complicated     62 (4)     66 (5)     0.017       Paralysis     15 (1)     15 (1)     0.001       Other neurologic disorders     61 (4)     81 (6)     0.068       Chronic pulmonary disease     216 (15)     204 (15)     0.017       Diabetes with chronic complications     14 (5)     77 (6)     0.013       Energy disease     29 (2)     46 (3)     0.068       Hypothyroidism     14 (2 (10)     154 (11)     0.033       Hypothyroidism     14 (2 (10)     154 (11)     0.031       Liver disease (bleeding)     2 (0)     1 (0)     0.021       AIDS     3 (0)     1 (0)     0.031       Liver disease (bleeding)     2 (0)     1 (0)     0.032       Metastatic cancer     152 (9)     130 (9)     0.017       Solid tumour without metastasis     321 (23)     272 (20)     <  | Vascular disease                                  | 57 (4)                     | 64 (5)                     | 0.027                                   |
| Initial of containing of contains and a section of a section | Pulmonary circulation disease                     | 69 (5)                     | 52 (A)                     | 0.027                                   |
| Tripping inclusion   50 (7)   50 (0)   0.010     Hypertension, complicated   50 (7)   60 (0)   0.017     Paralysis   15 (1)   15 (1)   0.017     Paralysis   15 (1)   15 (1)   0.017     Other neurologic disorders   61 (4)   81 (6)   0.068     Chronic pulmonary disease   216 (15)   204 (15)   0.018     Diabetes with chronic complications   33 (2)   46 (3)   0.058     Hypothyrioidism   142 (10)   154 (11)   0.033     Renal failure   74 (5)   77 (6)   0.013     Liver disease (bleding)   2 (0)   1 (0)   0.021     ADS   3 (0)   1 (0)   0.037     Lymphoma   29 (2)   29 (2)   0.002     Metastatic cancer   125 (9)   130 (9)   0.017     Solid tumour without metastasis   321 (23)   272 (20)   0.079     Rheumatoid arthritis/collagen vascular disease   60 (4)   65 (5)   0.020     Obesity   293 (21)   314 (23)   0.044     Weight loss   38 (3)   34 (2)   0.067   | Perinheral vascular disease                       | 98 (7)                     | 52 (4)<br>83 (6)           | 0.037                                   |
| Thypertension, uncomplicated     50° (20)     40° (20)     0.010       Hypertension, complicated     15 (1)     15 (1)     0.011       Paralysis     15 (1)     15 (1)     0.010       Other neurologic disorders     61 (4)     81 (6)     0.0068       Chronic pulmonary disease     216 (15)     204 (15)     0.018       Diabetes with chronic complications     145 (10)     136 (10)     0.013       Diabetes with chronic complications     142 (10)     154 (11)     0.033       Renal failure     74 (5)     77 (6)     0.013       Liver disease     39 (3)     30.002     200     100     0.021       ADS     30 (0)     1 (0)     0.033     100     100     0.033       Liver disease (bleeding)     2 (0)     1 (0)     0.037     100     0.022       MDS     30 (0)     1 (0)     0.037     100     0.037       Solid thronvirthout metastasis     321 (23)     272 (20)     0.007       Solid thronvirthout metastasis     321 (23)     373 (3)     0.007       <  | Hypertension uncomplicated                        | 507 (36)                   | 490 (35)                   | 0.040                                   |
| Instruction, complexitie     Del (a)     Del (b)     Del (b)       Paralysis     15 (1)     15 (1)     0001       Other neurologic disorders     61 (4)     81 (6)     0.068       Chronic pullomary disease     216 (15)     204 (15)     0.017       Diabetes with chronic complications     33 (2)     46 (3)     0.058       Hypothyroidism     142 (10)     154 (11)     0.033       Renal failure     74 (5)     77 (6)     0.013       Liver disease (bleeding)     2 (0)     1 (0)     0.0221       ADS     3 (0)     1 (0)     0.021       ADS     3 (0)     1 (0)     0.021 <t< td=""><td>Hypertension, complicated</td><td>62 (4)</td><td>-50 (55)<br/>66 (5)</td><td>0.013</td></t<>  | Hypertension, complicated                         | 62 (4)                     | -50 (55)<br>66 (5)         | 0.013                                   |
| The neurologic disorders     To (1)     To (1) <thto (1)<="" th=""></thto>  | Paralysis   | 15 (1)                     | 15 (1)                     | 0.017                                   |
| Other Natural Constraints     01 (1)     01 (0)     0.000       Dinabetes with out chronic complications     145 (10)     136 (10)     0.018       Diabetes with out chronic complications     33 (2)     46 (3)     0.058       Hypothyroidism     142 (10)     154 (11)     0.033       Renal failure     74 (5)     77 (6)     0.013       Liver disease     39 (3)     39 (3)     0.002       Peptic ulcer disease (bleeding)     2 (0)     1 (0)     0.021       ADS     3 (0)     1 (0)     0.037       Lymphoma     29 (2)     29 (2)     0.002       Metastatic cancer     125 (9)     130 (9)     0.017       Solid tumour without metastasis     321 (23)     272 (20)     0.020       Metastatic cancer     124 (8)     90 (7)     0.062       Coagulopathy     144 (8)     90 (7)     0.062       Obesity     293 (2)     37 (3)     0.007       Dificiency anaemias     384 (27)     358 (26)     0.034       Fluid and electrolyte disorders     589 (42)     576 (41)  | Other neurologic disorders                        | 61 (4)                     | 81 (6)                     | 0.001                                   |
| Diabetes with our openations     145 (10)     136 (10)     0.017       Diabetes with our openations     33 (2)     46 (3)     0.058       Hypothyroidism     142 (10)     154 (11)     0.033       Renal failure     74 (5)     77 (6)     0.013       Liver disease (bleeding)     2 (0)     1 (0)     0.021       ADS     3 (0)     1 (0)     0.033       Lymphoma     29 (2)     29 (2)     0.002       Metastatic cancer     125 (9)     130 (9)     0.017       Solid tumour without metastasis     321 (23)     272 (20)     0.002       Metastatic cancer     146 (6)     90 (7)     0.062       Coagulopathy     144 (8)     90 (7)     0.062       Obesity     293 (21)     314 (23)     0.044       Weight loss     384 (27)     358 (26)     0.034       Fluid and electrolyte disorders     589 (42)     576 (41)     0.007       Deficiency anaemia     39 (3)     37 (3)     0.007       Deficiency anaemia     38 (3)     34 (2)     0.057   | Chronic pulmonary disease                         | 216 (15)                   | 204 (15)                   | 0.000                                   |
| Diabetes with chronic complications     33 (2)     46 (3)     0.058       Hypothyroidism     142 (10)     154 (11)     0.033       Renal failure     74 (5)     77 (6)     0.013       Liver disease     39 (3)     39 (3)     0.002       Peptic ulcer disease (bleeding)     2 (0)     1 (0)     0.021       ADS     3 (0)     1 (0)     0.037       Lymphoma     29 (2)     29 (2)     0.002       Metastatic cancer     125 (9)     130 (9)     0.017       Solid tumour without metastasis     321 (23)     272 (20)     0.079       Rheumatoid arthritis/collagen vascular disease     60 (4)     65 (5)     0.020       Cagulopathy     114 (8)     90 (7)     0.062     0besity       Weight loss     38 (427)     358 (26)     0.034       Weight loss     39 (3)     37 (3)     0.007       Chronic blood loss anaemia     39 (3)     37 (3)     0.007       Dericiency anaemia     38 (3)     34 (2)     0.016       Psychoses     0 (6)     69 (5)     0.032  | Diabetes without chronic complications            | 145 (10)                   | 136 (10)                   | 0.017                                   |
| Hypothyriodism     12 (10)     15 (11)     0.033       Renal failure     74 (5)     77 (6)     0.013       Liver disease     39 (3)     39 (3)     0.002       Peptic ulcre disease (bleeding)     2 (0)     1 (0)     0.021       ADS     3 (0)     1 (0)     0.037       Lymphoma     29 (2)     29 (2)     0.002       Metastatic cancer     125 (9)     130 (9)     0.017       Solid tumour without metastasis     321 (23)     272 (20)     0.079       Rheumatoid arthritis/collagen vascular disease     60 (4)     65 (5)     0.020       Coagulopathy     114 (8)     90 (7)     0.062       Obesity     293 (21)     314 (23)     0.044       Weight loss     384 (27)     358 (26)     0.034       Fluid and electrolyte disorders     588 (42)     576 (41)     0.007       Chronic blood loss anaemia     39 (3)     37 (3)     0.007       Deficiency anaemias     388 (2)     24 (2)     0.016       Neyhoses     88 (3)     34 (2)     0.016   | Diabetes with chronic complications               | 33 (2)                     | 46 (3)                     | 0.058                                   |
| Program     T4 (6)     T7 (6)     0.013       Liver disease     39 (3)     39 (3)     0.002       Peptic ulcer disease (bleeding)     2 (0)     1 (0)     0.021       AIDS     3 (0)     1 (0)     0.037       Lymphoma     29 (2)     29 (2)     0.002       Metastatic cancer     125 (9)     130 (9)     0.017       Solid tumour without metastasis     321 (23)     272 (20)     0.079       Rheumatoid arthritis/collagen vascular disease     60 (4)     65 (5)     0.020       Obsity     293 (21)     314 (23)     0.044       Weight loss     384 (27)     358 (26)     0.034       Fluid and electrolyte disorders     589 (42)     576 (41)     0.007       Chronic blood loss anaemia     39 (3)     37 (3)     0.007       Deficiency anaemias     308 (22)     337 (24)     0.057       Alcohol abuse     28 (2)     29 (2)     0.007       Drug abuse     38 (3)     34 (2)     0.016       Psychoses     80 (6)     69 (5)     0.032   | Hypothyroidism                                    | 142 (10)                   | 154 (11)                   | 0.033                                   |
| Liver disease     39 (3)     39 (3)     0.002       Peptic ulcer disease (bleeding)     2 (0)     1 (0)     0.021       AIDS     3 (0)     1 (0)     0.037       Lymphoma     29 (2)     29 (2)     0.002       Metastatic cancer     125 (9)     130 (9)     0.017       Solid tumour without metastasis     321 (23)     272 (20)     0.020       Coagulopathy     114 (8)     90 (7)     0.062       Coagulopathy     114 (8)     90 (7)     0.062       Obesity     293 (21)     314 (23)     0.044       Weight loss     384 (27)     358 (26)     0.034       Fluid and electrolyte disorders     589 (42)     576 (41)     0.007       Chronic blood loss anaemia     39 (3)     37 (3)     0.007       Dericency anaemias     388 (3)     34 (2)     0.016       Psychoses     28 (2)     29 (2)     0.007       Drug abuse     28 (3)     34 (2)     0.016       Psychoses     28 (6)     623 (17)     232 (17)     0.019       P  | Renal failure                                     | 74 (5)                     | 77 (6)                     | 0.013                                   |
| Peptic ulcer disease (bleeding)     2 (0)     1 (0)     0.021       ADS     3 (0)     1 (0)     0.037       Lymphoma     29 (2)     29 (2)     0.002       Metastatic cancer     125 (9)     130 (9)     0.017       Solid tumour without metastasis     321 (23)     272 (20)     0.079       Rheumatoid arthritis/collagen vascular disease     60 (4)     65 (5)     0.020       Coagulopathy     114 (8)     90 (7)     0.062       Obesity     293 (21)     314 (23)     0.044       Weight loss     384 (27)     358 (26)     0.034       Fluid and electrolyte disorders     589 (42)     576 (41)     0.007       Chronic blood loss anaemia     39 (3)     37 (3)     0.007       Deficiency anaemias     308 (22)     337 (24)     0.057       Alcohol abuse     28 (2)     29 (2)     0.007       Drug abuse     38 (3)     34 (2)     0.016       Psychoses     80 (6)     69 (5)     0.032       Depression     245 (17)     232 (17)     0.019  | Liver disease                                     | 39 (3)                     | 39 (3)                     | 0.002                                   |
| ADS   3 (0)   1 (0)   0.037     Lymphoma   29 (2)   29 (2)   0.002     Metastatic cancer   125 (9)   130 (9)   0.017     Solid tumour without metastasis   321 (23)   272 (20)   0.079     Rheumatoid arthritis/collagen vascular disease   60 (4)   65 (5)   0.020     Coagulopathy   114 (8)   90 (7)   0.062     Obesity   293 (21)   314 (23)   0.044     Weight loss   384 (27)   358 (26)   0.033     Fluid and electrolyte disorders   589 (42)   576 (41)   0.007     Chronic blood loss anaemia   39 (3)   37 (3)   0.007     Deficiency anaemias   308 (22)   337 (24)   0.057     Alcohol abuse   28 (2)   29 (2)   0.007     Drug abuse   38 (3)   34 (2)   0.016     Psychoses   80 (6)   69 (5)   0.032     Depression   245 (17)   232 (17)   0.019     Primary diagnosis, No. (%)   71 (5)   73 (5)   676 (43)     Crohn disease   233 (17)   227 (16)   1007   | Peptic ulcer disease (bleeding)                   | 2 (0)                      | 1 (0)                      | 0.021                                   |
| Lymphoma     29 (2)     29 (2)     0.002       Metastatic cancer     125 (9)     130 (9)     0.017       Solid tumour without metastasis     321 (23)     272 (20)     0.079       Rheumatoid arthritis/collagen vascular disease     60 (4)     65 (5)     0.020       Coagulopathy     114 (8)     90 (7)     0.062       Obesity     233 (21)     314 (23)     0.044       Weight loss     384 (27)     358 (26)     0.034       Fluid and electrolyte disorders     589 (42)     576 (41)     0.007       Chronic blood loss anaemia     39 (3)     37 (3)     0.007       Deficiency anaemias     308 (22)     337 (24)     0.057       Alcohol abuse     28 (2)     29 (2)     0.007       Drug abuse     38 (3)     34 (2)     0.016       Psychoses     80 (6)     69 (5)     0.032       Depression     245 (17)     232 (17)     0.019       Cancer     676 (48)     642 (46)     642 (46)       Crohn disease     233 (17)     227 (16)     0.074  D   | AIDS  | 3 (0)                      | 1 (0)                      | 0.037                                   |
| Metastatic cancer     125 (9)     130 (9)     0.017       Solid tumour without metastasis     321 (23)     272 (20)     0.079       Rheumatoid arthritis/collagen vascular disease     60 (4)     65 (5)     0.020       Coagulopathy     114 (8)     90 (7)     0.062       Obesity     293 (21)     314 (23)     0.044       Weight loss     384 (27)     358 (26)     0.034       Fluid and electrolyte disorders     599 (42)     576 (41)     0.007       Chronic blood loss anaemia     399 (3)     37 (3)     0.007       Deficiency anaemias     308 (22)     337 (24)     0.057       Alcohol abuse     28 (2)     29 (2)     0.007       Drug abuse     38 (3)     34 (2)     0.016       Psychoses     80 (6)     69 (5)     0.032       Depression     245 (17)     232 (17)     0.019       Primary diagnosis, No. (%)     73 (5)     74       Cancer     676 (48)     642 (46)        Diverticulitis     154 (11)     155 (11)  | Lymphoma  | 29 (2)                     | 29 (2)                     | 0.002                                   |
| Solid tumour without metastasis     321 (23)     272 (20)     0.079       Rheumatoid arthritis/collagen vascular disease     60 (4)     65 (5)     0.020       Coagulopathy     114 (8)     90 (7)     0.062       Obesity     293 (21)     314 (23)     0.044       Weight loss     384 (27)     358 (26)     0.034       Fluid and electrolyte disorders     589 (42)     576 (41)     0.007       Chronic blood loss anaemia     39 (3)     37 (3)     0.007       Deficiency anaemias     308 (22)     337 (24)     0.057       Alcohol abuse     28 (2)     29 (2)     0.016       Psychoses     80 (6)     69 (5)     0.032       Depression     245 (17)     232 (17)     0.019       Primary diagnosis, No. (%)     71 (5)     73 (5)     0.074       Cancer     676 (48)     642 (46)     0.074       Diverticulitis     154 (11)     155 (11)     0.074       Ostomy     71 (5)     73 (5)     75 (51)       Fistula     98 (7)     113 (8)     1413 (8)     1  | Metastatic cancer                                 | 125 (9)                    | 130 (9)                    | 0.017                                   |
| Rheumatoid arthritis/collagen vascular disease     60 (4)     65 (5)     0.020       Coagulopathy     114 (8)     90 (7)     0.062       Obesity     293 (21)     314 (23)     0.044       Weight loss     384 (27)     358 (26)     0.034       Fluid and electrolyte disorders     589 (42)     576 (41)     0.007       Chronic blood loss anaemia     39 (3)     37 (3)     0.007       Deficiency anaemias     308 (22)     337 (24)     0.057       Alcohol abuse     28 (2)     29 (2)     0.007       Drug abuse     38 (3)     34 (2)     0.016       Psychoses     80 (6)     69 (5)     0.032       Depression     245 (17)     232 (17)     0.019       Primary diagnosis, No. (%)     71 (5)     73 (5)     0.074       Cancer     676 (48)     642 (46)   | Solid tumour without metastasis                   | 321 (23)                   | 272 (20)                   | 0.079                                   |
| Coagulopathy     114 (8)     90 (7)     0.062       Obesity     293 (21)     314 (23)     0.044       Weight loss     384 (27)     358 (26)     0.034       Fluid and electrolyte disorders     589 (42)     576 (41)     0.007       Chronic blood loss anaemia     39 (3)     37 (3)     0.007       Deficiency anaemias     308 (22)     337 (24)     0.057       Alcohol abuse     28 (2)     29 (2)     0.007       Drug abuse     38 (3)     34 (2)     0.016       Psychoses     80 (6)     69 (5)     0.032       Depression     245 (17)     232 (17)     0.019       Cancer     676 (48)     642 (46)     0.074       Cancer     676 (48)     642 (46)     0.074       Diverticulitis     154 (11)     155 (1)     0.074       Ostomy     71 (5)     73 (5)     73 (5)       Fistula     98 (7)     113 (8)     14       Hernia     24 (1)     30 (2)     0.074       Other     154 (11)     151 (12)   | Rheumatoid arthritis/collagen vascular disease    | 60 (4)                     | 65 (5)                     | 0.020                                   |
| Obesity     293 (21)     314 (23)     0.044       Weight loss     384 (27)     358 (26)     0.034       Fluid and electrolyte disorders     589 (42)     576 (41)     0.007       Chronic blood loss anaemia     39 (3)     37 (3)     0.007       Deficiency anaemias     308 (22)     337 (24)     0.057       Alcohol abuse     28 (2)     29 (2)     0.007       Drug abuse     38 (3)     34 (2)     0.016       Psychoses     80 (6)     69 (5)     0.032       Depression     245 (17)     232 (17)     0.019       Cancer     676 (48)     642 (46)        Cancer     676 (48)     642 (46)        Diverticulitis     154 (11)     155 (11)   | Coagulopathy                                      | 114 (8)                    | 90 (7)                     | 0.062                                   |
| Weight loss     384 (27)     358 (26)     0.034       Fluid and electrolyte disorders     589 (42)     576 (41)     0.007       Chronic blood loss anaemia     39 (3)     37 (3)     0.007       Deficiency anaemias     308 (22)     337 (24)     0.057       Alcohol abuse     28 (2)     29 (2)     0.007       Drug abuse     38 (3)     34 (2)     0.016       Psychoses     80 (6)     69 (5)     0.032       Depression     245 (17)     232 (17)     0.019       Primary diagnosis, No. (%)   | Obesity   | 293 (21)                   | 314 (23)                   | 0.044                                   |
| Fluid and electrolyte disorders   589 (42)   576 (41)   0.007     Chronic blood loss anaemia   39 (3)   37 (3)   0.007     Deficiency anaemias   308 (22)   337 (24)   0.057     Alcohol abuse   28 (2)   29 (2)   0.007     Drug abuse   38 (3)   34 (2)   0.016     Psychoses   80 (6)   69 (5)   0.032     Depression   245 (17)   232 (17)   0.019     Primary diagnosis, No. (%)   0.07   0.074   0.074     Cancer   676 (48)   642 (46)   0.074     Diverticulitis   154 (11)   155 (11)   0.074     Ostomy   71 (5)   73 (5)   73 (5)     Fistula   98 (7)   113 (8)   14     Hernia   24 (1)   30 (2)   14     Other   154 (11)   151 (12)   154 (11)   151 (12)     Preoperative oral antibiotic, No. (%)   773 (55)   765 (55)   0.003  | Weight loss                                       | 384 (27)                   | 358 (26)                   | 0.034                                   |
| Chronic blood loss anaemia     39 (3)     37 (3)     0.007       Deficiency anaemias     308 (22)     337 (24)     0.057       Alcohol abuse     28 (2)     29 (2)     0.007       Drug abuse     38 (3)     34 (2)     0.016       Psychoses     80 (6)     69 (5)     0.032       Depression     245 (17)     232 (17)     0.019       Primary diagnosis, No. (%)     7676 (48)     642 (46)     642 (46)       Cancer     676 (48)     642 (46)     642 (46)       Diverticulitis     154 (11)     155 (11)     155 (11)       Ostomy     71 (5)     73 (5)     73 (5)       Fistula     98 (7)     113 (8)     14       Hernia     24 (1)     30 (2)     154 (11)     151 (12)       Preoperative oral antibiotic, No. (%)     773 (55)     765 (55)     0.003  | Fluid and electrolyte disorders                   | 589 (42)                   | 576 (41)                   | 0.007                                   |
| Deficiency anaemias     308 (22)     337 (24)     0.057       Alcohol abuse     28 (2)     29 (2)     0.007       Drug abuse     38 (3)     34 (2)     0.016       Psychoses     80 (6)     69 (5)     0.032       Depression     245 (17)     232 (17)     0.019       Primary diagnosis, No. (%)      0.074     0.074       Cancer     676 (48)     642 (46)     642 (46)       Crohn disease     233 (17)     227 (16)     154 (11)     155 (11)       Ostomy     71 (5)     73 (5)     73 (5)     154 (11)     151 (12)       Preoperative oral antibiotic, No. (%)     773 (55)     765 (55)     0.003       Preoperative powel prenaration medication No. (%)     773 (55)     765 (55)     0.003   | Chronic blood loss anaemia                        | 39 (3)                     | 37 (3)                     | 0.007                                   |
| Alcohol abuse   28 (2)   29 (2)   0.007     Drug abuse   38 (3)   34 (2)   0.016     Psychoses   80 (6)   69 (5)   0.032     Depression   245 (17)   232 (17)   0.019     Primary diagnosis, No. (%)  | Deficiency anaemias                               | 308 (22)                   | 337 (24)                   | 0.057                                   |
| Drug abuse   38 (3)   34 (2)   0.016     Psychoses   80 (6)   69 (5)   0.032     Depression   245 (17)   232 (17)   0.019     Primary diagnosis, No. (%)  | Alcohol abuse                                     | 28 (2)                     | 29 (2)                     | 0.007                                   |
| Psychoses   80 (6)   69 (5)   0.032     Depression   245 (17)   232 (17)   0.019     Primary diagnosis, No. (%)   | Drug abuse  | 38 (3)                     | 34 (2)                     | 0.016                                   |
| Depression     245 (17)     232 (17)     0.019       Primary diagnosis, No. (%)     0.074     0.074       Cancer     676 (48)     642 (46)     642 (46)       Crohn disease     233 (17)     227 (16)     154 (11)     155 (11)       Diverticulitis     154 (11)     155 (11)     154 (11)     155 (11)       Ostomy     71 (5)     73 (5)     73 (5)     113 (8)       Hernia     24 (1)     30 (2)     154 (11)     151 (12)       Preoperative oral antibiotic, No. (%)     773 (55)     765 (55)     0.003       Preoperative powel preparation medication No. (%)     363 (26)     327 (24)     0.052   | Psychoses   | 80 (6)                     | 69 (5)                     | 0.032                                   |
| Primary diagnosis, No. (%)     0.074       Cancer     676 (48)     642 (46)       Crohn disease     233 (17)     227 (16)       Diverticulitis     154 (11)     155 (11)       Ostomy     71 (5)     73 (5)       Fistula     98 (7)     113 (8)       Hernia     24 (1)     30 (2)       Other     154 (11)     151 (12)       Preoperative oral antibiotic, No. (%)     773 (55)     765 (55)     0.003   | Depression  | 245 (17)                   | 232 (17)                   | 0.019                                   |
| Cancer   676 (48)   642 (46)     Crohn disease   233 (17)   227 (16)     Diverticulitis   154 (11)   155 (11)     Ostomy   71 (5)   73 (5)     Fistula   98 (7)   113 (8)     Hernia   24 (1)   30 (2)     Other   154 (11)   151 (12)     Preoperative oral antibiotic, No. (%)   773 (55)   765 (55)   0.003  | Primary diagnosis, No. (%)                        | 070 (40)                   | 0.40 (40)                  | 0.074                                   |
| Cronn disease   233 (17)   227 (16)     Diverticulitis   154 (11)   155 (11)     Ostomy   71 (5)   73 (5)     Fistula   98 (7)   113 (8)     Hernia   24 (1)   30 (2)     Other   154 (11)   151 (12)     Preoperative oral antibiotic, No. (%)   773 (55)   765 (55)   0.003   | Cancer  | 676 (48)                   | 642 (46)                   |   |
| Diversion     154 (11)     155 (11)       Ostomy     71 (5)     73 (5)       Fistula     98 (7)     113 (8)       Hernia     24 (1)     30 (2)       Other     154 (11)     151 (12)       Preoperative oral antibiotic, No. (%)     773 (55)     765 (55)     0.003       Preoperative powel preparation medication No. (%)     363 (26)     327 (24)     0.052  | Cronn uisease                                     | 233 (17)                   | 227 (16)                   |   |
| Usionity     (1 (5)     (73 (5)       Fistula     98 (7)     113 (8)       Hernia     24 (1)     30 (2)       Other     154 (11)     151 (12)       Preoperative oral antibiotic, No. (%)     773 (55)     765 (55)     0.003       Preoperative powel preparation medication No. (%)     363 (26)     327 (24)     0.052   | Diverticulitis                                    | 154 (11)                   | 155 (11)                   |   |
| Fisure     98 (/)     113 (8)       Hernia     24 (1)     30 (2)       Other     154 (11)     151 (12)       Preoperative oral antibiotic, No. (%)     773 (55)     765 (55)     0.003       Preoperative howel prenaration medication. No. (%)     363 (26)     327 (24)     0.052   | Usturiiy  | / 1 (5)                    | 13 (5)                     |   |
| Terma     24 (1)     30 (2)       Other     154 (11)     151 (12)       Preoperative oral antibiotic, No. (%)     773 (55)     765 (55)     0.003       Preoperative howel prenaration medication. No. (%)     363 (26)     327 (24)     0.052  | Fistula   | 98 ( <i>1</i> )            | IIJ (δ)                    |   |
| Outer     134 (11)     151 (12)       Preoperative oral antibiotic, No. (%)     773 (55)     765 (55)     0.003       Preoperative howel preparation medication No. (%)     363 (26)     327 (24)     0.052   | Othor   | 24 (1)                     | 3U (Z)                     |   |
| Preoperative lowel preparation medication No. (%) (30) (30) (30) (30) (30) (30) (30) (30  | Ulici<br>Preoperative oral antihiotic No. (0/)    | 104 (11)<br>779 (EE)       | 101 (12)<br>765 (FE)       | 0.002                                   |
| - COMPARING TO THE STATE STA  | Preoperative bowel preparation medication No. (%) | 363 (26)                   | 327 (24)                   | 0.003                                   |

| Table A2. | Baseline and Intraoperative | Factors for the First Operation | of Ohio Patients (N = 2,801) |
|-----------|-----------------------------|---------------------------------|------------------------------|
|-----------|-----------------------------|---------------------------------|------------------------------|

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(Continued)

#### Table A2. (Continued)

|  |                    | 20% Ovugon        | Absolute<br>Standardized |
|--|--------------------|-------------------|--------------------------|
| Variables  | (N = 1.410)        | (N = 1, 391)      | Difference*              |
|  | \                  |                   |                          |
| Type of surgery, No. (%)   |                    |                   | 0.093                    |
| Colorectal resection   | 892 (63)           | 841 (61)          |                          |
| Lower gastrointestinal therapeutic procedures                      | 295 (21)           | 304 (22)          |                          |
| Small bowel resection  | 85 (6)             | 96 (7)            |                          |
| Exploratory laparotomy   | 24 (2)             | 37 (2)            |                          |
| Excision   | 22 (2)             | 21 (2)            |                          |
| Laparoscopy  | 31 (2)             | 33 (2)            |                          |
| Hernia repair  | 24 (2)             | 24 (2)            |                          |
| lleostomy and other enterostomy                                    | 17 (1)             | 20 (1)            |                          |
| Colostomy  | 20 (1)             | 15 (1)            |                          |
| Laparoscopic surgery (vs. open or converted), No. (%)              | 485 (34)           | 450 (32)          | 0.043                    |
| Duration of surgery, h   | 4.3 ± 1.7          | $4.4 \pm 1.8$     | 0.027                    |
| Regional block, No. (%)  | 29 (2)             | 40 (3)            | 0.053                    |
| Spinal or epidural anesthesia, No. (%)                             | 112 (8)            | 125 (9)           | 0.037                    |
| Attending anesthesiologist, + No. (%)                              |                    |                   | —‡                       |
| A  | 182 (13)           | 180 (13)          |                          |
| В  | 194 (14)           | 178 (13)          |                          |
| C  | 48 (3)             | 77 (6)            |                          |
| D  | 74 (5)             | 41 (3)            |                          |
|  | 32 (2)             | 43 (3)            |                          |
| Operating room number, No. (%)                                     | 000 (00)           | 000 (00)          | 0.062                    |
| #47  | 323 (23)           | 308 (22)          |                          |
| #48  | 317 (23)           | 299 (21)          |                          |
| #50  | 261 (19)           | 266 (19)          |                          |
| #46  | 194 (14)           | 191 (14)          |                          |
| #45  | 191 (14)           | 201 (15)          |                          |
| #49  | 68 (5)             | 79 (6)            |                          |
| #40-44   | 56 (4)             | 47 (3)            |                          |
| Intraoperative management  |                    |                   |                          |
| Time-weighted average of esophageal                                |                    |                   |                          |
| temperature, °C  | $36.0 \pm 0.6$ §   | $36.0 \pm 0.6 \ $ | 0.077                    |
| Esophageal temperature at end of case, °C                          | 36.4 [35.9, 36.8]§ | 36.4 [35.9, 36.8] | 0.021                    |
| Time-weighted average of MAP, mmHg                                 | 87 ± 9             | 86 ± 9            | 0.112                    |
| Time-weighted average of HR, beats/min                             | 76 ± 11            | 78 ± 12           | 0.094                    |
| Amount of anesthetic gas (MAC), h                                  | 3.1 [2.2, 4.2] #   | 3.1 [2.1, 4.3]**  | 0.030                    |
| Fraction of inspired oxygen, %                                     | 80 [78, 82]        | 39 [35, 48]       | 3.132                    |
| Time-weighted average of PETCO <sub>2</sub> , mmHg                 | 35 ± 2             | 35 ± 2            | 0.016                    |
| Time-weighted average of glucose, mg/dl                            | 142 [122, 164]††   | 141 [120, 165]‡‡  | 0.041                    |
| Crystalloid volume, I  | 2.8 [2.1, 3.6]     | 2.9 [2.1, 3.7]    | 0.024                    |
| Laparoscopic surgery   | 2.8 [2.2, 3.4]     | 2.8 [2.2, 3.5]    |                          |
| Open surgery   | 2.9 [2.0, 3.8]     | 2.9 [2.0, 3.8]    | 0.000                    |
| Collola Volume, I  | 0 [0, 0.5]         | 0 [0, 0.5]        | 0.092                    |
| Esumateu biolog loss, mi   | 100 [50, 250]      | 100 [50, 250]     | 0.040                    |
| BIOOU (Fallslusion, No. (%)  |                    | 131 (9)           | 0.005                    |
| Amount of blood transitision among patients who were transfused, I | 0.7 [0.4, 1.0]     | 0.7 [0.4, 1.0]    | 0.005                    |

Summary statistics (presented as % of patients, mean ± SD, or median [25th, 75th percentiles], respectively, for factors, symmetric continuous variables, and skewed continuous variables).

\*Absolute standardized difference: absolute difference in means or proportions divided by the pooled SD. Any baseline or procedural variables with an absolute standardized difference greater than 0.10 was considered to be imbalanced and would be adjusted for in the analysis. †Five attending anesthesiologists (of 64) with most cases are listed, due to the limited space. ‡Absolute standardized difference was not calculated due to too many categories (among 64 anesthesiologists). §A total of 57 cases have missing data. #IA total of 45 cases have missing data. #A total of 952 cases have missing data. #t total of 911 cases have missing data.

AIDS, acquired immune deficiency syndrome; ASA, American Society of Anesthesiologists; HR, heart rate; MAC, minimal alveolar concentration; MAP, mean arterial blood pressure; PETCO<sub>2</sub>, end-tidal pressure of carbon dioxide.

| Table A3. | Baseline and Int | raoperative Factor | s for the Last | Operation of | of Ohio | Patients | (N = | 2,801 | ) |
|-----------|------------------|--------------------|----------------|--------------|---------|----------|------|-------|---|
|-----------|------------------|--------------------|----------------|--------------|---------|----------|------|-------|---|

| Ape, yr     56 ± 17     54 ± 17     0.073       Ferrale     739 (52)     725 (52)       Broz, No, Yo,     0.663       White     125 (89)     1207 (87)       Back, No, Yo,     122 (9)     136 (1)       Back, No, Yo,     132 (9)     137 (23)     0.152       Barding, Satan, Xo, Wo,     25 (2)     27 (23, 31)     0.123       Charding, Satan, Xo, Wo,     0.133     0.123     0.123       Charding, Satan, Xo, Wo,     0.134     0.134     0.123       Charding, Satan, Xo, Wo,     0.132     0.12     0.12       Charding, Satan, Xo, Wo,     0.134     0.134     0.134       Charding, Satan, Xo, Wo,     0.132     0.12     0.12       Charding, Satan, Xo, Wo,     0.12     0.12     0.12       Applied, Satan, Xo, Wo,     0.12     0.12     0.12       I     6 (1)     6 (1)     6 (1)     0.131       Warding, Satan, Xo, Wo,     2.00     0.01     0.011       I     12 (1)     7 (1)     0.221       J <td< th=""><th>Variables</th><th>80% Oxygen<br/>(N = 1, 412)</th><th>30% Oxygen<br/>(N = 1, 389)</th><th>Absolute<br/>Standardized<br/>Difference*</th></td<>   | Variables  | 80% Oxygen<br>(N = 1, 412) | 30% Oxygen<br>(N = 1, 389) | Absolute<br>Standardized<br>Difference* |
|---|--|----------------------------|----------------------------|---|
| Gender, No, Yeb, Centrol     755 (62)       Male     757 (42)     664 (40)       Back, No, Yeb, Centrol     0.033       White     1225 (89)     1227 (27)       Back, No, Yeb, Centrol     25 (2)     26 (2)       Back, No, Yeb, Centrol     25 (2)     26 (2)       Back, No, Yeb, Centrol     26 (2)     26 (2)       Back, No, Yeb, Centrol     11 (4)     18 (2)       Back, No, Yeb, Centrol     11 (4)     18 (2)       Back, No, Yeb, Centrol     11 (4)     18 (2)       Back, No, Yeb, Centrol     10 (1)     10 (1)       Centrol     11 (4)     139 (2)     322 (2)       II     399 (2)     399 (2)     322 (2)       II     399 (2)     322 (2)     00 (2)       V     20 (2)     00     10       V     20 (2)     00     128 (9)       V     20 (2)     128 (9)     128 (9)       V     20 (2) (1) (1) (2) (2)     139 (2) (1) (2) (2)       And Statistic Statistic Statistic Statistic Statistic Statistic Statististic Statististic Statistic Statistic Statistic Statistic Stati   | Age, yr  | 56 ± 17                    | 54 ± 17                    | 0.073                                   |
| Fendale     739 (52)     725 (52)       Bace, No (%)     0.033       White     125 (69)     1207 (87)       Black     122 (9)     156 (1)       Other     252 (2)     28 (2)       Boy mass index, kpln*1     26 (23, 31)     27 (23, 31)     0.012       Schwing status, No, (%)     131 (30)     418 (30)     148 (30)       Exernoler     191 (14)     136 (1)     150 (1)     1002       Rest macher     191 (14)     136 (1)     150 (1)     1002       Rest macher     191 (14)     138 (1)     150 (1)     1002       Rest macher     67 (5)     68 (5) (5)     100 (1)       V     200     0.00     100       V     200     0.001     1002       Valutard valutar disease     63 (5)     67 (4)     0.031       Valutar disease     70 (5)     57 (4)     0.021       Valutar disease     63 (5)     67 (6)     0.041       Parity associal disorders     76 (5)     76 (6)     0.010       Valutar disease   | Gender, No. (%)                                    |                            |                            | 0.003                                   |
| Male     673 (48)     664 (48)       Nuth     1255 (89)     1277 (87)       White     1255 (89)     127 (23, 21)       Other     25 (2)     26 (2)       Bock     25 (2)     26 (2)       Bock     191 (14)     136 (10)     127 (23, 31)       Current smoker     191 (14)     136 (10)     127 (23, 31)       Ex-smoker     191 (14)     136 (10)     13       Ex-smoker     191 (14)     136 (10)     14       Ex-smoker     191 (14)     136 (10)     1002       Image: Status, No. (%)     507 (62)     502 (62)     14       Image: Status, No. (%)     130 (9)     128 (9)     100       Image: Status, No. (%)     130 (9)     128 (9)     100       V     130 (9)     128 (9)     100     100       V     130 (9)     128 (14)     0.059     11     0.031       V     130 (9)     127 (7)     91 (7)     0.071       V     130 (9)     137 (14)     0.059       Parbirari Vascatus dis   | Female   | 739 (52)                   | 725 (52)                   |   |
| nable, Name     0.0053       While     1255 (89)     1220 (87)       Back     122 (9)     158 (11)       Other     252 (2)     26 (2)       Back     121 (9)     158 (11)       Other     25 (2)     26 (2)     0.012       Schwalls, No, Yoh     0.123     0.012       Chrent smoker     131 (40)     418 (30)       Exernolet     131 (40)     418 (30)       Exernolet     313 (30)     418 (30)       Adversal status, No, Yoh     0.002     0.002       I     6(1)     6(1)     0.002       I     6(1)     6(1)     0.013       V     200     0     V       Vaccuta disease     70 (5)     57 (4)     0.031       Vaccuta disease     19 (1)<  |  | 673 (48)                   | 664 (48)                   | 0.000                                   |
| max     12.2 (m)     1.20 (m)       Other     25 (c)     26 (c)       Body mask index, kg m <sup>2</sup> 26 (c)     27 (c), 31     27 (c), 31       Current standor     191 (14)     35 (10)     413 (10)     418 (10)       Current standor     790 (56)     353 (10)     418 (10)     414 (10)       New standor     790 (56)     352 (20)     400 (10)     414 (10)       Ad hysical status, No. (%)     6 (1)     <   | Kace, No. (%)                                      | 1255 (80)                  | 1207 (07)                  | 0.063                                   |
| Other     25 [2]     26 [2, 31]     27 [23, 31]     0.102       Smoking status, No. (%)     26 [23, 31]     27 [23, 31]     0.123       Durrent smoker     191 (14)     18 (10)     1.123       Newer smoker     431 (120)     481 (20)     1.123       Newer smoker     790 (86)     835 (60)     600       ASA physical status, No. (%)     6(1)     6(1)     0.002       I     390 (28)     932 (28)     932 (28)       Vi     330 (9)     128 (9)     V       Visit of disease     67 (5)     57 (4)     0.041       Pulmonary (relates     67 (5)     57 (4)     0.059       Vasciar disease     102 (7)     91 (7)     0.012       Pulmonary (relates without complication     526 (57)     478 (8)     0.059       Hypertensitur, complication     74 (5)     500     0.21       Dither meurologic disorders </td <td>Black</td> <td>132 (9)</td> <td>156 (11)</td> <td></td>   | Black  | 132 (9)                    | 156 (11)                   |   |
| Body mass index, kg/m <sup>2</sup> 21 (23, 31)     21 (23, 31)     0.123       Durrent smoker     191 (14)     136 (10)     1.33       Durrent smoker     190 (16)     835 (60)     0.002       ASA physical status, No. (%)     6 (1)     6 (1)     0.002       II     399 (28)     392 (28)     0.002       III     399 (28)     392 (28)     0.002       V     130 (9)     128 (9)     0       V     2 (0)     0 (0)     0.013       Vacatar disease     35 (5)     6 1 (4)     0.003       Patimonary circutation disease     120 (7)     31 (7)     0.027       Patimonary circutation disea   | Other  | 25 (2)                     | 26 (2)                     |   |
| Smoking status, No. (%)     91 (14)     136 (10)       Ex-emotor     431 (30)     418 (30)       Never smoker     431 (30)     418 (30)       ASA physical status, No. (%)     0.002     0.002       ASA physical status, No. (%)     6 (1)     6 (1)     6 (1)       I     399 (26)     853 (60)     1       Never smoker     737 (62)     853 (62)     N       V     20)     0 (0)     1       Medical history, No. (%)     20)     0 (0)     1       Vancular disease     73 (5)     57 (4)     0.031       Puminary circulation disease     70 (5)     57 (4)     0.041       Propheral vascular disease     70 (5)     78 (6)     0.010       Other neurologic disorders     76 (5)     78 (6)     0.021       Diabetes with otronic complications     33 (3)     46 (3)<   | Body mass index, kg/m <sup>2</sup>                 | 26 [23, 31]                | 27 [23, 31]                | 0.012                                   |
| Current studier     191 (14)     136 (10)       Kexmaker     790 (56)     835 (60)       ASA physical status, No. (%)     0.002       I     6 (1)     6 (1)       III     6 (7)     6 (1)       III     875 (52)     392 (23)       III     875 (52)     835 (62)       V     2 (0)     0 (0)       Medical history, No. (%)     2 (0)     0 (0)       Congestive heart failure     57 (5)     57 (4)     0.003       Vascular disease     70 (5)     57 (4)     0.001       Vascular disease     70 (5)     57 (4)     0.001       Peripheral vascular disease     70 (5)     57 (4)     0.013       Vascular disease     70 (5)     57 (4)     0.016       Paripheral vascular disease     70 (5)     78 (6)     0.010       Congestive heart failure     22 (16)     209 (15)     0.016       Diabetes with concic complications     146 (10)     134 (11)     0.021       Diabetes with concic complications     146 (10)     144 (11)     0.024  | Smoking status, No. (%)                            |                            |                            | 0.123                                   |
| LX-SIN06rf   410 (30)   416 (30)     ASA priscal status, No. (%)   0.002     I   6 (1)   6 (1)     III   399 (28)   392 (28)     IIII   399 (28)   392 (28)     IV   130 (9)   128 (9)     V   2 (0)   0.001     Medical history, No. (%)   70 (6 (5 )   57 (4)   0.031     Vacular disease   63 (6)   61 (4)   0.003     Vacular disease   63 (6)   57 (4)   0.041     Patimonary circulation disease   70 (6 (5 7 (4))   0.059     Hypertension, complicated   71 (5)   67 (5)   0.059     Hypertension, complicated   71 (5)   67 (6)   0.010     Chrone uncomplications   13 (1)   13 (1)   0.039     Other neurologic disorders   76 (6)   76 (6)   0.024     Diabetes with chronic complications   14 (10)   154 (11)   0.024     Internet of the chronic complications   33 (3)   46 (3)   0.033     Diabetes with chronic complications   33 (2)   40 (3)   0.033     Diabetes with chronic complications   | Current smoker                                     | 191 (14)                   | 136 (10)                   |   |
| Image     Part (b)     So (b)     So (b)       I     6 (1)     6 (1)     6 (1)       II     393 (28)     392 (28)       III     875 (62)     683 (62)       V     2 (0)     0 (0)       Medical history No. (%)     2 (0)     0 (0)       V     2 (0)     0 (0)       Vascular disease     67 (5)     57 (4)     0.031       Vascular disease     70 (5)     57 (4)     0.041       Peripheral vascular disease     70 (5)     57 (4)     0.059       Hypertansion, complicated     71 (5)     67 (5)     0.003       Peripheral vascular disease     70 (5)     57 (4)     0.059       Hypertansion, complicated     71 (5)     67 (5)     0.003       Peripheral vascular disease     72 (6)     209 (15)     0.021       Diabetes without chronic complications     14 (10)     13 (1)     0.036       Hypertanizer     78 (6)     78 (6)     0.010       Diabetes without chronic complications     33 (2)     46 (3)     0.036       Hypothymi   | EX-SMOKEr  | 431 (30)                   | 418 (30)                   |   |
| International Net (%)     6 (1)     6 (1)     6 (1)       II     399 (28)     392 (28)     392 (28)       III     399 (28)     393 (28)     392 (28)       V     130 (9)     128 (8)     V       V     2 (0)     0 (0)       Medical disease     67 (6)     57 (4)     0.031       Vascular disease     63 (6)     61 (4)     0.0031       Vascular disease     70 (6)     57 (4)     0.041       Peripheral vascular disease     70 (6)     57 (4)     0.041       Peripheral vascular disease     12 (7)     91 (7)     0.027       Phypertension, complicated     76 (6)     78 (6)     0.010       Chronic pulmonary disease     228 (16)     209 (15)     0.021       Diabates with out chronic complications     14 (6 (10)     154 (11)     0.024       Renal failure     80 (6)     80 (6)     80 (6)     0.003       Liver disease (bleeding)     2 (0)     100     0.021     0.003       Paptic lucer disease (bleeding)     2 (0)     100     0.024  | ASA nhysical status. No. (%)                       | 790 (56)                   | 635 (60)                   | 0.002                                   |
| ii     399 (29)     392 (28)       iii     875 (62)     863 (62)       V     130 (8)     128 (8)       V     2(0)     0(0)       Medical history, No. (%)     67 (5)     57 (4)     0.031       Vascular disease     63 (5)     51 (4)     0.0031       Pulmonary circulation disease     70 (5)     57 (4)     0.041       Peripheral vascular disease     70 (5)     57 (4)     0.041       Peripheral vascular disease     70 (5)     57 (4)     0.041       Peripheral vascular disease     70 (5)     57 (4)     0.041       Preipheral vascular disease     70 (5)     78 (6)     0.009       Paralysis     19 (1)     13 (1)     0.033       Other neurologic disorders     76 (5)     78 (6)     0.010       Diabetes without chronic complications     14 (10)     15 (10)     0.016       Diabetes without chronic complications     38 (3)     46 (3)     0.033       Hend failure     80 (6)     80 (6)     0.004       Luer disease (heeting)     20 (1)     10 (0)<   |  | 6 (1)                      | 6 (1)                      | 0.002                                   |
| III     875 (62)     863 (62)       V     130 (9)     128 (9)       V     2 (0)     0 (0)       Medical history, No. (%)  | II.  | 399 (28)                   | 392 (28)                   |   |
| IV     130 (9)     128 (9)       V     2(0)     0(0)       Medical history, No. (%)     -     -       Congestive heart failure     63 (5)     61 (4)     0.031       Vascular disease     63 (5)     57 (4)     0.041       Peripheral vascular disease     102 (7)     91 (7)     0.027       Hypertension, complicated     71 (5)     57 (5)     0.009       Pariphary vascular disease     122 (7)     91 (7)     0.027       Hypertension, complicated     71 (5)     57 (5)     0.009       Pariphary vascular disease     76 (5)     78 (6)     0.010       Other neurologic disorders     76 (5)     78 (6)     0.021       Diabetes with chronic complications     145 (10)     136 (10)     0.016       Diabetes with chronic complications     146 (10)     154 (11)     0.024       Renal failure     80 (6)     80 (6)     0.004       Liver disease     40 (3)     40 (3)     0.033       Particuter disease (bleeding)     20 (10)     0.037     0.011       Liver disease (blee  | Ш  | 875 (62)                   | 863 (62)                   |   |
| V     2 (0)     0.0)       Medical history, No. (%)     0.031       Congestive heart failure     67 (5)     57 (4)     0.031       Vascular disease     63 (5)     61 (4)     0.003       Pulmonary circulation disease     70 (5)     57 (4)     0.041       Peripheral vascular disease     102 (7)     91 (7)     0.027       Hypertension, complicated     526 (37)     478 (34)     0.059       Paralysis     19 (1)     13 (1)     0.039       Other neurologic disorders     76 (5)     78 (6)     0.010       Chronic pulmorary disease     223 (16)     209 (15)     0.021       Diabetes with chronic complications     145 (10)     136 (10)     0.016       Diabetes with chronic complications     146 (10)     154 (11)     0.024       Renal failure     80 (6)     80 (6)     0.004       Liver disease (bleeding)     10     0.037     0     100     0.037       Jupportoridism     146 (10)     154 (11)     0.024     0.036     0.036     0.036     0.037     0.037 <t< td=""><td>IV</td><td>130 (9)</td><td>128 (9)</td><td></td></t<>  | IV   | 130 (9)                    | 128 (9)                    |   |
| Medical instary, No. (%)     67 (5)     57 (4)     0.031       Vascular disease     63 (5)     51 (4)     0.003       Vascular disease     70 (5)     57 (4)     0.041       Peripheral vascular disease     102 (7)     91 (7)     0.027       Hypertension, uncomplicated     71 (5)     67 (5)     0.009       Paralysis     19 (1)     13 (1)     0.039       Other neurologic disorders     78 (5)     78 (6)     0.010       Chronic pulmonary disease     223 (16)     299 (15)     0.021       Diabetes with chronic complications     145 (10)     154 (11)     0.016       Diabetes with chronic complications     38 (3)     46 (3)     0.036       Hypothyroidism     146 (10)     154 (11)     0.024       Luer disease     0.06     80 (6)     0.004       Luer diseases     2.00     1.00     0.021       ADS     3.00     1.00     0.021       ADS     3.00     1.00     0.037       Salid tumour without metastasis     326 (23)     269 (20)     0.091 <td>V M F H H H M (0)</td> <td>2 (0)</td> <td>0 (0)</td> <td></td>   | V M F H H H M (0)                                  | 2 (0)                      | 0 (0)                      |   |
| Consistence from them taken taken to be approximated in the taken t | Medical history, No. (%)                           | 67 (5)                     | 57 (1)                     | 0.021                                   |
| Dumonary circulation disease     Do (b)     D (c)     D (c)     D (c)     D (c)     D (c)       Purimenary circulation disease     102 (7)     91 (7)     0.027       Hypertension, complicated     52 (637)     476 (34)     0.059       Hypertension, complicated     71 (5)     67 (5)     0.009       Paralysis     19 (1)     13 (1)     0.033       Other neurologic disorders     76 (5)     78 (6)     0.010       Chronic pulmonary disease     223 (16)     209 (15)     0.021       Diabetes with chronic complications     38 (3)     46 (3)     0.038       Hypothyroldism     146 (10)     154 (11)     0.024       Renal failure     80 (6)     80 (6)     0.003       Liver disease     40 (3)     40 (3)     0.003       Peptic ulter disease (bleeding)     2 (0)     1 (0)     0.037       Lymphona     33 (2)     25 (2)     0.038       Metastatic cancer     124 (9)     137 (10)     0.037       Solid tumour without metastasis     326 (23)     269 (20)     0.091   | Vascular disease                                   | 67 (5)                     | 57 (4)<br>61 (4)           | 0.031                                   |
| Peripheral vascular disease     102 (7)     91 (7)     0.027       Hypertension, uncomplicated     526 (37)     478 (34)     0.059       Hypertension, complicated     77 (5)     67 (5)     0.009       Paralysis     19 (1)     13 (1)     0.039       Other neurologic disorders     76 (5)     78 (6)     0.010       Chronic pulmonary disease     223 (16)     209 (15)     0.021       Diabetes without chronic complications     145 (10)     136 (10)     0.016       Diabetes without chronic complications     38 (3)     46 (3)     0.036       Hypothypoldism     146 (10)     154 (11)     0.024       Renal failure     80 (6)     80 (6)     0.004       Liver disease     040 (3)     40 (3)     0.033       Peptic ulcer disease (bleeding)     2 (0)     1 (0)     0.021       JLV     30 (0)     1 (0)     0.037       Liver disease     66 (5)     64 (5)     0.003       Solid turnour without metastasis     326 (23)     289 (20)     0.091       Rematoid arthrit/scollagen vascular disease   | Pulmonary circulation disease                      | 70 (5)                     | 57 (4)                     | 0.041                                   |
| Hypertension, uncomplicated     526 (37)     478 (34)     0.059       Hypertension, complicated     71 (5)     67 (5)     0.009       Paralysis     19 (1)     13 (1)     0.039       Other neurologic disorders     76 (6)     78 (6)     0.010       Chronic pulmonary disease     223 (16)     209 (15)     0.021       Diabetes with our chronic complications     145 (10)     136 (10)     0.016       Diabetes with our chronic complications     38 (3)     46 (3)     0.036       Hypothyroidism     146 (10)     154 (11)     0.024       Renal failure     80 (6)     80 (6)     0.004       Liver disease     40 (3)     40 (3)     0.037       Jymphoma     33 (2)     25 (2)     0.038       Lymphoma     33 (2)     25 (2)     0.037       Solid tumoru without metastasis     326 (23)     269 (20)     0.091       Renal taiture     16 (6)     64 (5)     0.0037       Solid tumoru without metastasis     326 (23)     269 (20)     0.091       Remat taiture     36 (3)     42  | Peripheral vascular disease                        | 102 (7)                    | 91 (7)                     | 0.027                                   |
| Hypertension; complicated     71 (5)     67 (5)     0.009       Paralysis     19 (1)     13 (1)     0.039       Other neurologic disorders     76 (5)     78 (6)     0.010       Chronic pulmonary disease     223 (16)     209 (15)     0.021       Diabetes with chronic complications     145 (10)     136 (10)     0.036       Hypothyroidism     146 (10)     154 (11)     0.024       Renal failure     80 (6)     80 (6)     0.004       Liver disease     40 (3)     40 (3)     0.003       Peptic ulcer disease (bleeding)     2 (0)     1 (0)     0.021       AIDS     3 (0)     1 (0)     0.037       Lymphoma     33 (2)     2 5 (2)     0.038       Metastatic cancer     124 (9)     137 (10)     0.037       Solid tumour without metastasis     226 (23)     269 (20)     0.091       Rheumatol architekschalls cancer     156 (6)     64 (5)     0.003       Cacaguopathy     296 (21)     334 (24)     0.074       Weight loss     39 (3)     42 (3)     0.016  | Hypertension, uncomplicated                        | 526 (37)                   | 478 (34)                   | 0.059                                   |
| Paralysis   19 (1)   13 (1)   0.039     Other neurologic disorders   76 (5)   78 (6)   0.010     Chronic pulmonary disease   223 (16)   209 (15)   0.021     Diabetes without chronic complications   145 (10)   136 (10)   0.016     Diabetes without chronic complications   38 (3)   46 (3)   0.036     Hypothyroidism   146 (10)   154 (11)   0.024     Renal railure   80 (6)   80 (6)   0.004     Liver disease   40 (3)   40 (3)   0.003     Peptic ulcer disease (bleeding)   2 (0)   1 (0)   0.021     AIDS   30 (0)   1 (0)   0.037     Lymphoma   33 (2)   25 (2)   0.038     Metastatic cancer   124 (9)   137 (10)   0.037     Solid tumour without metastasis   326 (23)   269 (20)   0.091     Rheumatoid arthritis/collagen vascular disease   66 (5)   64 (5)   0.003     Coagulopathy   15 (8)   104 (8)   0.024   0.074     Weight loss   405 (29)   335 (28)   0.005     Fluid and electrolyle disorders  | Hypertension, complicated                          | 71 (5)                     | 67 (5)                     | 0.009                                   |
| Under Neurologic disorders     76 (b)     76 (b)     0.010       Chronic pulmonary disease     223 (16)     209 (15)     0.021       Diabetes with our chronic complications     145 (10)     136 (10)     0.016       Diabetes with our chronic complications     38 (3)     46 (3)     0.036       Hypothyroidism     146 (10)     154 (11)     0.024       Renal failure     80 (6)     80 (6)     0.003       Liver disease     40 (3)     40 (3)     0.003       Peptic ulcer disease (bleeding)     2 (0)     1 (0)     0.021       AIDS     3 (0)     1 (0)     0.037       Sold tumour without metastasis     326 (23)     269 (20)     0.091       Retauntatio distribution     326 (23)     269 (20)     0.003       Coaquipoatiny     151 (8)     104 (8)     0.024       Obesity     296 (21)     334 (24)     0.074       Weight loss     405 (29)     395 (28)     0.005       Fuid and electrolyte disorders     635 (45)     628 (45)     0.005       Fuid and electrolyte disorders     39 (3)   | Paralysis  | 19 (1)                     | 13 (1)                     | 0.039                                   |
| Diablets   23 (10)   20 (11)   0.021     Diablets   145 (10)   136 (10)   0.036     Diablets   38 (3)   46 (3)   0.036     Hypothyroidism   146 (10)   154 (11)   0.024     Renal failure   80 (6)   80 (6)   0.004     Liver disease   40 (3)   40 (3)   0.003     Peptic ulcer disease (bleeding)   2 (0)   1 (0)   0.037     AIDS   3 (0)   1 (0)   0.037     Lymphoma   33 (2)   25 (2)   0.038     Metastatic cancer   124 (9)   137 (10)   0.037     Solid tumour without metastasis   326 (23)   269 (20)   0.091     Rheumatoid arthritis/collagen vascular disease   66 (5)   64 (5)   0.003     Coagulogathy   115 (8)   104 (8)   0.024   0.024     Obesity   296 (21)   334 (24)   0.074   0.035     Chronic blood loss anaemia   39 (3)   42 (3)   0.016   0.055     Chronic blood loss anaemia   39 (3)   42 (3)   0.016   0.065     Diverticultitis   39 (3) <td>Uther neurologic disorders</td> <td>/b (5)<br/>222 (16)</td> <td>78 (6)<br/>200 (15)</td> <td>0.010</td>  | Uther neurologic disorders                         | /b (5)<br>222 (16)         | 78 (6)<br>200 (15)         | 0.010                                   |
| Diabetes with chronic complications     38 (3)     46 (3)     0.036       Hypothyroidism     146 (10)     154 (11)     0.024       Renal failure     80 (6)     80 (6)     0.004       Liver disease     40 (3)     40 (3)     0.003       Peptic ulcer disease (bleeding)     2 (0)     1 (0)     0.037       Lymphoma     33 (2)     25 (2)     0.038       Metastatic cancer     124 (9)     137 (10)     0.037       Solid tumour without metastasis     326 (23)     269 (20)     0.091       Rheumatoid arthrtis/collagen vascular disease     66 (5)     64 (5)     0.003       Caagulopathy     115 (8)     104 (8)     0.024       Obesity     296 (21)     334 (24)     0.074       Weight loss     405 (29)     395 (28)     0.005       Chronic blood loss anaemia     339 (3)     42 (3)     0.016       Deficiency anaemias     339 (24)     355 (26)     0.036       Alcohol abuse     30 (2)     31 (2)     0.007       Drug abuse     30 (2)     31 (2)     0.007 <td>Diabetes without chronic complications</td> <td>145 (10)</td> <td>136 (10)</td> <td>0.021</td>   | Diabetes without chronic complications             | 145 (10)                   | 136 (10)                   | 0.021                                   |
| Hypothyroidism   146 (10)   154 (11)   0.024     Renal failure   80 (6)   80 (6)   0.004     Liver disease   40 (3)   40 (3)   0.003     Peptic ulcer disease (bleeding)   2 (0)   1 (0)   0.021     AIDS   3 (0)   1 (0)   0.037     Lymphoma   33 (2)   25 (2)   0.038     Metastatic cancer   124 (9)   137 (10)   0.037     Solid tumour without metastasis   326 (23)   269 (20)   0.091     Rheumatoid arthritis/collagen vascular disease   66 (5)   64 (5)   0.003     Coagulopathy   115 (8)   104 (8)   0.024     Obesity   296 (21)   334 (24)   0.074     Weight loss   405 (29)   395 (28)   0.005     Fluid and electrolyte disorders   635 (45)   628 (45)   0.0037     Deficiency anaemias   339 (24)   355 (26)   0.036     Alcohol abuse   30 (2)   31 (2)   0.007     Drug abuse   30 (2)   31 (2)   0.007     Program   296 (19)   242 (17)   0.037 <t< td=""><td>Diabetes with chronic complications</td><td>38 (3)</td><td>46 (3)</td><td>0.036</td></t<>   | Diabetes with chronic complications                | 38 (3)                     | 46 (3)                     | 0.036                                   |
| Renal failure     80 (6)     80 (6)     0.004       Liver disease     40 (3)     40 (3)     0.003       Liver disease (bleeding)     2 (0)     1 (0)     0.021       AIDS     3 (0)     1 (0)     0.037       Lymphoma     33 (2)     25 (2)     0.038       Metastatic cancer     124 (9)     137 (10)     0.037       Solid tumour without metastasis     226 (23)     266 (20)     0.091       Rheumatoid arthritis/collagen vascular disease     66 (5)     64 (5)     0.003       Coagulopathy     296 (21)     334 (24)     0.074       Weight loss     405 (29)     395 (28)     0.005       Fluid and electrolyte disorders     635 (45)     628 (45)     0.005       Chronic blod loss anaemia     39 (3)     42 (3)     0.016       Deficiency anaemias     339 (24)     355 (26)     0.036       Actohalause     39 (3)     40 (3)     0.007       Psychoses     80 (6)     79 (6)     0.001       Depression     266 (19)     242 (17)     0.037  P   | Hypothyroidism                                     | 146 (10)                   | 154 (11)                   | 0.024                                   |
| Liver disease     40 (3)     40 (3)     0.003       Peptic ulcer disease (bleeding)     2 (0)     1 (0)     0.021       AIDS     3 (0)     1 (0)     0.037       Lymphoma     33 (2)     25 (2)     0.038       Metastatic cancer     124 (9)     137 (10)     0.037       Solid tumour without metastasis     326 (23)     269 (20)     0.091       Rheumatoid arthritis/collagen vascular disease     66 (5)     64 (5)     0.003       Cagulopathy     115 (8)     104 (8)     0.024       Obesity     296 (21)     334 (24)     0.074       Weight loss     405 (29)     395 (28)     0.005       Fluid and electrolyte disorders     635 (45)     628 (45)     0.005       Chronic blood loss anaemia     39 (3)     40 (3)     0.007       Drug abuse     39 (3)     40 (3)     0.007       Pry abuse     39 (3)     40 (3)     0.007       Pry abuse     39 (3)     40 (3)     0.007       Pry abuse     39 (3)     40 (3)     0.001       Depre   | Renal failure                                      | 80 (6)                     | 80 (6)                     | 0.004                                   |
| Peptic ulcer disease (bleeding)   2 (0)   1 (0)   0.021     AIDS   3 (0)   1 (0)   0.037     Lymphoma   33 (2)   25 (2)   0.038     Metastatic cancer   124 (9)   137 (10)   0.037     Solid turnour without metastasis   326 (23)   269 (20)   0.091     Rheumatolid arthritis/collagen vascular disease   66 (5)   64 (5)   0.003     Coagulopathy   115 (8)   104 (8)   0.024     Obesity   296 (21)   334 (24)   0.074     Weight loss   405 (29)   395 (28)   0.005     Chronic blood loss anaemia   39 (3)   42 (3)   0.016     Deficiency anaemias   339 (24)   355 (26)   0.036     Alcohol abuse   30 (2)   31 (2)   0.007     Drug abuse   39 (3)   40 (3)   0.007     Primary diagnosis, No. (%)   266 (19)   242 (17)   0.037     Cancer   662 (47)   612 (44)   0.065     Cancer   662 (47)   612 (44)   0.065     Chrind isease   219 (16)   233 (17)   0.065   | Liver disease                                      | 40 (3)                     | 40 (3)                     | 0.003                                   |
| AUS   3 (0)   1 (0)   0.037     Lymphoma   33 (2)   25 (2)   0.038     Metastatic cancer   124 (9)   137 (10)   0.037     Solid tumour without metastasis   326 (23)   269 (20)   0.091     Rheumatoid arthritis/collagen vascular disease   66 (5)   64 (5)   0.003     Cagulopathy   115 (8)   104 (8)   0.024     Obesity   296 (21)   334 (24)   0.074     Weight loss   405 (29)   395 (28)   0.005     Fluid and electrolyte disorders   635 (45)   628 (45)   0.005     Chronic blood loss anaemia   39 (3)   42 (3)   0.016     Deficiency anaemias   39 (24)   355 (26)   0.036     Alcohol abuse   30 (2)   31 (2)   0.007     Drug abuse   39 (3)   40 (3)   0.007     Psychoses   80 (6)   79 (6)   0.001     Depression   266 (19)   242 (17)   0.037     Primary diagnosis, No. (%)   108 (7)   117 (8)   0.065     Cancer   662 (47)   612 (44)   0.014 <td< td=""><td>Peptic ulcer disease (bleeding)</td><td>2 (0)</td><td>1 (0)</td><td>0.021</td></td<>  | Peptic ulcer disease (bleeding)                    | 2 (0)                      | 1 (0)                      | 0.021                                   |
| Description   35 (2)   2.5 (2)   0.030     Metastatic cancer   124 (9)   137 (10)   0.037     Solid tumour without metastasis   326 (23)   269 (20)   0.091     Rheumatoid arthritis/collagen vascular disease   66 (5)   64 (5)   0.003     Coagulopathy   115 (8)   104 (8)   0.024     Obesity   296 (21)   334 (24)   0.074     Weight loss   405 (29)   395 (28)   0.005     Chronic blood loss anaemia   39 (3)   42 (3)   0.016     Deficiency anaemias   339 (24)   355 (26)   0.036     Alcohol abuse   30 (2)   31 (2)   0.007     Drug abuse   39 (3)   40 (3)   0.007     Psychoses   80 (6)   79 (6)   0.001     Depression   266 (19)   242 (17)   0.037     Orind disease   219 (16)   233 (17)   0.065     Cancer   662 (47)   612 (44)   612 (44)     Crohn disease   219 (16)   233 (17)   0.065     Diverticulitis   147 (10)   145 (10)   145 (10)   145 (10)   | AIDS   | 3 (U)<br>33 (2)            | I (U)<br>25 (2)            | 0.037                                   |
| Solid tumour without metastasis   121 (c)   | Metastatic cancer                                  | 124 (9)                    | 137 (10)                   | 0.030                                   |
| Rheumatoid arthritis/collagen vascular disease   66 (5)   64 (5)   0.003     Coagulopathy   115 (8)   104 (8)   0.024     Obesity   296 (21)   334 (24)   0.074     Weight loss   405 (29)   395 (28)   0.005     Fluid and electrolyte disorders   635 (45)   628 (45)   0.005     Chronic blood loss anaemia   39 (3)   42 (3)   0.016     Deficiency anaemias   339 (24)   355 (26)   0.036     Alcohol abuse   39 (3)   40 (3)   0.007     Pry abuse   39 (3)   40 (3)   0.007     Psychoses   30 (2)   31 (2)   0.007     Psychoses   80 (6)   79 (6)   0.001     Depression   266 (19)   242 (17)   0.037     Cancer   662 (47)   612 (44)   0.065     Cancer   662 (47)   612 (44)   0.065     Cancer   662 (37)   97 (6)   0.011     Diverticulitis   147 (10)   145 (11)   0.055     Other   198 (7)   177 (8)   177 (8)     Fistula   36 (3)  | Solid tumour without metastasis                    | 326 (23)                   | 269 (20)                   | 0.091                                   |
| Coagulopathy     115 (8)     104 (8)     0.024       Obesity     296 (21)     334 (24)     0.074       Weight loss     405 (29)     395 (28)     0.005       Fluid and electrolyte disorders     635 (45)     628 (45)     0.005       Chronic blood loss anaemia     39 (3)     42 (3)     0.016       Deficiency anaemias     339 (24)     355 (26)     0.036       Alcohol abuse     30 (2)     31 (2)     0.007       Drug abuse     39 (3)     40 (3)     0.007       Psychoses     80 (6)     79 (6)     0.001       Depression     266 (19)     242 (17)     0.037       Primary diagnosis, No. (%)     662 (47)     612 (44)     600       Cancer     662 (47)     612 (44)     648 (47)     0.015       Diverticulitis     147 (10)     145 (11)     56 (7)     7 (7)       Hernia     36 (3)     40 (3)     616 (3)     40 (3)       Other     145 (10)     145 (10)     145 (10)       Preoperative oral antibiotic, No. (%)     672 (48)     64   | Rheumatoid arthritis/collagen vascular disease     | 66 (5)                     | 64 (5)                     | 0.003                                   |
| Obesity     296 (21)     334 (24)     0.074       Weight loss     405 (29)     395 (28)     0.005       Fluid and electrolyte disorders     635 (45)     628 (45)     0.005       Chronic blood loss anaemia     39 (3)     42 (3)     0.016       Deficiency anaemias     339 (24)     355 (26)     0.036       Alcohol abuse     30 (2)     31 (2)     0.007       Drug abuse     39 (3)     40 (3)     0.007       Psychoses     80 (6)     79 (6)     0.001       Depression     266 (19)     242 (17)     0.037       Primary diagnosis, No. (%)     0     0.065     0.065       Cancer     662 (47)     612 (44)     0.065       Castomy     108 (7)     117 (8)     0.065       Primary diagnosis, No. (%)     108 (7)     97 (7)     145 (10)       Ostomy     108 (7)     97 (7)     145 (10)     145 (10)       Preoperative oral antibiotic, No. (%)     672 (48)     648 (47)     0.019       Preoperative bowel preparation medication, No. (%)     313 (22)     275 (20   | Coagulopathy                                       | 115 (8)                    | 104 (8)                    | 0.024                                   |
| Weight loss     405 (29)     395 (28)     0.005       Fluid and electrolyte disorders     635 (45)     628 (45)     0.005       Chronic blood loss anaemia     39 (3)     42 (3)     0.016       Deficiency anaemias     339 (24)     355 (26)     0.036       Alcohol abuse     30 (2)     31 (2)     0.007       Drug abuse     39 (3)     40 (3)     0.007       Psychoses     80 (6)     79 (6)     0.001       Depression     266 (19)     242 (17)     0.037       Primary diagnosis, No. (%)     0.065     0.065     0.065       Cancer     662 (47)     612 (44)     0.065       Cancer     147 (10)     145 (11)     0.065       Diverticulitis     147 (10)     145 (11)     145 (11)       Ostomy     108 (7)     117 (8)     145 (10)       Fistula     95 (7)     97 (7)     145 (10)       Hernia     36 (3)     40 (3)     0.019       Other     145 (10)     145 (10)     145 (10)       Preoperative oral antibiotic, No. (%)  | Obesity  | 296 (21)                   | 334 (24)                   | 0.074                                   |
| Findla and detectory disorders   633 (45)   626 (45)   0.005     Chronic blood loss anaemia   39 (3)   42 (3)   0.016     Deficiency anaemias   339 (24)   355 (26)   0.036     Alcohol abuse   30 (2)   31 (2)   0.007     Drug abuse   39 (3)   40 (3)   0.007     Psychoses   80 (6)   79 (6)   0.001     Depression   266 (19)   242 (17)   0.037     Primary diagnosis, No. (%)   0.065   0.065   0.065     Cancer   662 (47)   612 (44)   0.065     Cancer   662 (47)   612 (44)   0.065     Diverticulitis   147 (10)   145 (11)   0.055     Ostomy   108 (7)   117 (8)   117     Fistula   95 (7)   97 (7)   117     Hernia   36 (3)   40 (3)   0.019     Other   145 (10)   145 (10)   145 (10)     Preoperative oral antibiotic, No. (%)   672 (48)   648 (47)   0.019     Preoperative bowel preparation medication, No. (%)   313 (22)   275 (20)   0.058   | Weight loss  | 405 (29)                   | 395 (28)                   | 0.005                                   |
| Deficiency anaemias   33 (24)   355 (26)   0.036     Alcohol abuse   30 (2)   31 (2)   0.007     Drug abuse   39 (3)   40 (3)   0.007     Psychoses   80 (6)   79 (6)   0.001     Depression   266 (19)   242 (17)   0.037     Primary diagnosis, No. (%)   0.065   0.065   0.065     Cancer   662 (47)   612 (44)   0.065     Cancer   662 (47)   612 (44)   0.065     Diverticulitis   147 (10)   145 (11)   0.065     Ostomy   108 (7)   117 (8)   117 (8)     Fistula   95 (7)   97 (7)   145 (10)     Hernia   36 (3)   40 (3)   0.019     Other   145 (10)   145 (10)   145 (10)     Preoperative oral antibiotic, No. (%)   672 (48)   648 (47)   0.019     Preoperative bowel preparation medication, No. (%)   313 (22)   275 (20)   0.058   | Fluid and electrolyte disorders                    | 035 (45)<br>30 (3)         | 628 (45)<br>12 (3)         | 0.005                                   |
| Alcohol abuse   30 (2)   31 (2)   0.007     Drug abuse   39 (3)   40 (3)   0.007     Psychoses   80 (6)   79 (6)   0.001     Depression   266 (19)   242 (17)   0.037     Primary diagnosis, No. (%)   0   0   0   0.065     Cancer   662 (47)   612 (44)   0.065     Crohn disease   219 (16)   233 (17)   0.057     Diverticulitis   147 (10)   145 (11)   0     Ostomy   108 (7)   117 (8)   117     Fistula   95 (7)   97 (7)   145 (10)     Hernia   36 (3)   40 (3)   0     Other   145 (10)   145 (10)   145 (10)     Preoperative oral antibiotic, No. (%)   672 (48)   648 (47)   0.019     Preoperative bowel preparation medication, No. (%)   313 (22)   275 (20)   0.058   | Deficiency anaemias                                | 339 (24)                   | 355 (26)                   | 0.036                                   |
| Drug abuse   39 (3)   40 (3)   0.007     Psychoses   80 (6)   79 (6)   0.001     Depression   266 (19)   242 (17)   0.037     Primary diagnosis, No. (%)   0   0   0.065     Cancer   662 (47)   612 (44)     Crohn disease   219 (16)   233 (17)     Diverticulitis   147 (10)   145 (11)     Ostomy   108 (7)   117 (8)     Fistula   95 (7)   97 (7)     Hernia   36 (3)   40 (3)     Other   145 (10)   145 (10)     Preoperative oral antibiotic, No. (%)   672 (48)   648 (47)   0.019     Preoperative bowel preparation medication, No. (%)   313 (22)   275 (20)   0.058   | Alcohol abuse                                      | 30 (2)                     | 31 (2)                     | 0.007                                   |
| Psychoses   80 (6)   79 (6)   0.001     Depression   266 (19)   242 (17)   0.037     Primary diagnosis, No. (%)   0   0.065     Cancer   662 (47)   612 (44)     Crohn disease   219 (16)   233 (17)     Diverticulitis   147 (10)   145 (11)     Ostomy   108 (7)   117 (8)     Fistula   95 (7)   97 (7)     Hernia   36 (3)   40 (3)     Other   145 (10)   145 (10)     Preoperative oral antibiotic, No. (%)   672 (48)   648 (47)   0.019     Preoperative bowel preparation medication, No. (%)   313 (22)   275 (20)   0.058  | Drug abuse   | 39 (3)                     | 40 (3)                     | 0.007                                   |
| Depression   266 (19)   242 (17)   0.037     Primary diagnosis, No. (%)   0.065     Cancer   662 (47)   612 (44)     Crohn disease   219 (16)   233 (17)     Diverticulitis   147 (10)   145 (11)     Ostomy   108 (7)   117 (8)     Fistula   95 (7)   97 (7)     Hernia   36 (3)   40 (3)     Other   145 (10)   145 (10)     Preoperative oral antibiotic, No. (%)   672 (48)   648 (47)   0.019     Preoperative bowel preparation medication, No. (%)   313 (22)   275 (20)   0.058  | Psychoses  | 80 (6)                     | 79 (6)                     | 0.001                                   |
| Primary diagnosis, No. (%)   0.065     Cancer   662 (47)   612 (44)     Crohn disease   219 (16)   233 (17)     Diverticulitis   147 (10)   145 (11)     Ostomy   108 (7)   117 (8)     Fistula   95 (7)   97 (7)     Hernia   36 (3)   40 (3)     Other   145 (10)   145 (10)     Preoperative oral antibiotic, No. (%)   672 (48)   648 (47)   0.019     Preoperative bowel preparation medication, No. (%)   313 (22)   275 (20)   0.058   | Depression   | 266 (19)                   | 242 (17)                   | 0.037                                   |
| Caliber   662 (47)   612 (44)     Crohn disease   219 (16)   233 (17)     Diverticulitis   147 (10)   145 (11)     Ostomy   108 (7)   117 (8)     Fistula   95 (7)   97 (7)     Hemia   36 (3)   40 (3)     Other   145 (10)   145 (10)     Preoperative oral antibiotic, No. (%)   672 (48)   648 (47)   0.019     Preoperative bowel preparation medication, No. (%)   313 (22)   275 (20)   0.058  | Primary diagnosis, No. (%)                         | 660 (47)                   | 610 (14)                   | 0.065                                   |
| Contributes   213 (10)   233 (17)     Diverticulitis   147 (10)   145 (11)     Ostomy   108 (7)   117 (8)     Fistula   95 (7)   97 (7)     Hernia   36 (3)   40 (3)     Other   145 (10)   145 (10)     Preoperative oral antibiotic, No. (%)   672 (48)   648 (47)   0.019     Preoperative bowel preparation medication, No. (%)   313 (22)   275 (20)   0.058   | Crohn disease                                      | 002 (47)                   | 012 (44)                   |   |
| Ostomy   108 (7)   117 (8)     Fistula   95 (7)   97 (7)     Hernia   36 (3)   40 (3)     Other   145 (10)   145 (10)     Preoperative oral antibiotic, No. (%)   672 (48)   648 (47)   0.019     Preoperative bowel preparation medication, No. (%)   313 (22)   275 (20)   0.058  | Diverticulitis                                     | 147 (10)                   | 145 (11)                   |   |
| Fistula     95 (7)     97 (7)       Hemia     36 (3)     40 (3)       Other     145 (10)     145 (10)       Preoperative oral antibiotic, No. (%)     672 (48)     648 (47)     0.019       Preoperative bowel preparation medication, No. (%)     313 (22)     275 (20)     0.058  | Ostomy   | 108 (7)                    | 117 (8)                    |   |
| Hernia     36 (3)     40 (3)       Other     145 (10)     145 (10)       Preoperative oral antibiotic, No. (%)     672 (48)     648 (47)     0.019       Preoperative bowel preparation medication, No. (%)     313 (22)     275 (20)     0.058   | Fistula  | 95 (7)                     | 97 (7)                     |   |
| Other     145 (10)     145 (10)       Preoperative oral antibiotic, No. (%)     672 (48)     648 (47)     0.019       Preoperative bowel preparation medication, No. (%)     313 (22)     275 (20)     0.058  | Hernia   | 36 (3)                     | 40 (3)                     |   |
| Preoperative oral antibiotic, No. (%)     672 (48)     648 (47)     0.019       Preoperative bowel preparation medication, No. (%)     313 (22)     275 (20)     0.058  | Other  | 145 (10)                   | 145 (10)                   |   |
| Preoperative power preparation medication, No. (%) 313 (22) 2/5 (20) 0.058  | Preoperative oral antibiotic, No. (%)              | 672 (48)                   | 648 (47)                   | 0.019                                   |
|   | rieoperative power preparation medication, No. (%) | 313 (22)                   | 275 (20)                   | 0.058                                   |

#### Table A3. (Continued)

| Variables   | 80% Oxygen<br>(N = 1, 412) | 30% Oxygen<br>(N = 1, 389) | Absolute<br>Standardized<br>Difference* |
|---|----------------------------|----------------------------|---|
|   | (=.,)                      | (                          |   |
| Type of surgery, No. (%)  |                            |                            | 0.096                                   |
| Colorectal resection  | 753 (53)                   | 709 (51)                   |   |
| Lower gastrointestinal therapeutic procedures                     | 426 (30)                   | 433 (31)                   |   |
| Small bowel resection   | 74 (5)                     | 83 (6)                     |   |
| Exploratory laparotomy  | 29 (2)                     | 44 (3)                     |   |
| Excision  | 27 (2)                     | 21 (2)                     |   |
| Laparoscopy   | 33 (2)                     | 29 (2)                     |   |
| Hernia repair   | 37 (3)                     | 35 (3)                     |   |
| lleostomy and other enterostomy                                   | 18 (1)                     | 22 (2)                     |   |
| Colostomy   | 15 (1)                     | 13 (1)                     |   |
| Laparoscopic surgery (vs. open or converted), No. (%)             | 401 (28)                   | 365 (26)                   | 0.048                                   |
| Duration of surgery, h  | 4.1 ± 1.7                  | 4.1 ± 1.8                  | 0.008                                   |
| Regional block, No. (%)   | 33 (2)                     | 43 (3)                     | 0.047                                   |
| Spinal or epidural anesthesia, No. (%)                            | 106 (8)                    | 109 (8)                    | 0.013                                   |
| Attending anesthesiologist, † No. (%)                             |                            |                            | —‡                                      |
| Α   | 191 (14)                   | 179 (13)                   |   |
| В   | 187 (13)                   | 185 (13)                   |   |
| C   | 61 (4)                     | 83 (6)                     |   |
| D   | 65 (5)                     | 41 (3)                     |   |
| E   | 28 (2)                     | 43 (3)                     |   |
| Operating room number, No. (%)                                    |                            |                            | 0.100                                   |
| #47   | 310 (22)                   | 283 (20)                   |   |
| #48   | 290 (20)                   | 263 (19)                   |   |
| #50   | 250 (18)                   | 271 (20)                   |   |
| #46   | 216 (15)                   | 215 (16)                   |   |
| #45   | 210 (15)                   | 217 (16)                   |   |
| #49   | 73 (5)                     | 91 (6)                     |   |
| #40-44  | 63 (5)                     | 49 (3)                     |   |
| Intraoperative management   |                            |                            |   |
| Time-weighted average of esophageal                               |                            |                            |   |
| temperature, °C   | $36.0 \pm 0.6$ §           | $36.0 \pm 0.6$             | 0.054                                   |
| Esophageal temperature at end of case, °C                         | 36.4 [35.9, 36.8] §        | 36.3 [35.8, 36.8]          | 0.010                                   |
| Time-weighted average of MAP, mmHg                                | 86 ± 9                     | 85 ± 9                     | 0.093                                   |
| Time-weighted average of HR, beats/min                            | 76 ± 11                    | 77 ± 11                    | 0.154                                   |
| Amount of anesthetic gas (MAC), h                                 | 2.9 [2.0, 4.0] #           | 2.8 [1.9, 4.0] **          | 0.037                                   |
| Fraction of inspired oxygen. %                                    | 80 [78, 82]                | 39 [35, 47]                | 3.095                                   |
| Time-weighted average Perco., mmHg                                | $35 \pm 2$                 | $35 \pm 2$                 | 0.018                                   |
| Time-weighted average of glucose. mg/dl                           | 141 [121, 163]++           | 139 [117, 164]±±           | 0.060                                   |
| Crystalloid volume. I   | 2.6 [1.9. 3.4]             | 2.6 [1.8, 3.5]             | 0.011                                   |
| Laparoscopic surgery  | 2.7 [2.1, 3.3]             | 2.7 [2.1, 3.4]             |   |
| Open surgery  | 2.5 [1.7, 3.5]             | 2.6 [1.7, 3.5]             |   |
| Colloid volume, I   | 0 [0, 0.25]                | 0 [0, 0.5]                 | 0.103                                   |
| Estimated blood loss, ml  | 100 [50, 200]              | 100 [50, 200]              | 0.038                                   |
| Blood transfusion, No. (%)  | 108 (7.6)                  | 109 (7.8)                  | 0.007                                   |
| Amount of blood transfusion among patients who were transfused, I | 0.6 [0.3, 1.0]             | 0.7 [0.4, 1.0]             | 0.009                                   |

Summary statistics (presented as % of patients, mean ± SD, or median [25th, 75th percentiles], respectively, for factors, symmetric continuous variables, and skewed continuous variables).

\*Absolute standardized difference: absolute difference in means or proportions divided by the pooled SD. Any baseline or procedural variables with an absolute standardized difference greater than 0.10 was considered to be imbalanced and would be adjusted for in the analysis. †Five attending anesthesiologists (of 64) with most cases are listed, due to the limited space. ‡Absolute standardized difference was not calculated due to too many categories (among 64 anesthesiologists). §A total of 64 cases have missing data. #A total of 51 cases have missing data. #One case has missing data. \*Five cases have missing data. ††A total of 1,018 cases have missing data. ‡t total of 970 cases have missing data.

AIDS, acquired immune deficiency syndrome; ASA, American Society of Anesthesiologists; HR, heart rate; MAC, minimal alveolar concentration; MAP, mean arterial blood pressure; PETCO<sub>2</sub>, end-tidal pressure of carbon dioxide.