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ORIGINAL ARTICLE

Complications and Their Association with Mortality Following Emergency Gastrointestinal Surgery—an Observational Study

Anders Winther Voldby[1] · Anders Watt Boolsen[1] · Anne Albers Aaen[2] · Jakob Burcharth[5] · Sarah Ekeløf[5] · Roberto Loprete[3] · Simon Jønck[4] · Hassan Ali Eskandarani[2] · Lau Caspar Thygesen[6] · Ann Merete Møller[7] · Birgitte Brandstrup[1]

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Abstract

Purpose Emergency gastrointestinal surgery is followed by a high risk of major complications and death. This study aimed to investigate which complications showed the strongest association with death following emergency surgery for gastrointestinal obstruction or perforation.

Methods We retrospectively included adults who had undergone emergency gastrointestinal surgery for radiologically verified obstruction or perforation at three Danish hospitals between 2014 and 2015. The exposure variables comprised 16 predefined Clavien-Dindo-graded complications. Cox regression with delayed entry was used to analyze the association of these complications with 90-day mortality. We adjusted for hospital, age, American Society of Anesthesiologists classification, pre-operative Sepsis-2 score, cardiac comorbidity, renal comorbidity, hypertension, active cancer, bowel obstruction or perforation, and the surgical procedure. Subgroup analyses were done for patients with gastrointestinal obstruction or perforation.

Results Of the 349 included patients, 281 (80.5%) experienced at least one complication. The risk of death was 20.6% (14) for patients with no complications and varied between 21 and 57% for patients with complications. Renal impairment (hazard ratio (HR): 6.8 (95%CI: 3.7–12.4)), arterial thromboembolic events (HR 4.8 (2.3–9.9)), and atrial fibrillation (HR 4.4 (2.8–6.8)) showed the strongest association with 90-day mortality. Atrial fibrillation was the only complication significantly associated with death in patients with gastrointestinal obstruction as well as perforation.

Conclusion This study of patients undergoing emergency gastrointestinal surgery revealed that renal impairment, arterial thromboembolic events, and atrial fibrillation had the strongest association with death. Atrial fibrillation may serve as an in-situ marker of patients needing escalation of care.

Keywords Gastrointestinal diseases · Emergency · Perioperative care · Complications · Outcomes

Introduction

Emergency abdominal surgery is followed by a substantial risk of postoperative complications which influence the risk of death of 15–25%.[1–3] Complications develop in over 30% of patients and vary according to patient characteristics, hospital characteristics, and the underlying pathology.[4–6] Adverse events often prolong the hospital stay, and postoperative complications are more strongly associated with mortality than are pre- and intra-operative variables.[7,8] A recent study found

✉ Anders Winther Voldby
anders.voldby@gmail.com

1 Department of Surgery, Holbæk Hospital, Part of Copenhagen University Hospitals, Smedelundsgade 60, 4300 Holbaek, Denmark

2 Department of Anesthesiology and Intensive Care Medicine, Holbæk Hospital, Holbæk, Denmark

3 Department of Surgery, Slagelse Hospital, Slagelse, Denmark

4 Department of Emergency Medicine, Holbæk Hospital, Holbæk, Denmark

5 Department of Surgery, Zealand University Hospital, Roskilde, Denmark

6 Department of Population Health and Morbidity, University of Southern Denmark, Odense, Denmark

7 Department of Anesthesiology and Intensive Care Medicine, Herlev Hospital, Herlev, Denmark

major complications in 47% of patients following emergency laparotomy for gastrointestinal obstruction, perforation, or bleeding and a mortality risk of 26%.[9] The risk of major cardiac and pulmonary complications was high the first days after surgery as was the risk of death. However, little is known about which postoperative complications are most strongly associated with death following emergency gastrointestinal (GI) surgery.

The association between postoperative complications and death has been addressed in several cohorts within elective surgery. The risk of death in patients with major postoperative complications is referred to as failure-to-rescue (FTR). FTR has proven to be effective for evaluating the postoperative course at an institutional level because it allows for the development of post hoc protocols to optimize care. Although the FTR metric was originally developed for planned surgical procedures with a low risk of complications or death,[10] it has recently been gaining ground in emergency surgery,[11–14] and thus, its use is extending to patient with other diagnoses. Moreover, the incidence, type, and severity of complications following emergency surgery may differ considerably from those of elective cohorts and is likely to affect the association between specific complications and death. Importantly, specific postoperative complications may serve as valuable in situ markers of when to escalate care to prevent a fatal outcome.

Different complications appear at different times throughout the postoperative course, as does death. As such, the association between a complication and death needs to take into account the time without a complication (unexposed) and the time from a debuting complication to death (exposed). Not taking this into account may lead to what is known as "immortal time bias." Taking into consideration the "unexposed" and the "exposed" time may add important understanding of the association between individual complications and death following an eventful course of emergency GI surgery.

We hypothesized that complications evolve in continuums and that certain complications are more strongly associated with 90-day mortality than others following emergency GI surgery. Further to this, some complications may serve as markers of an evolving adverse course independently of the underlying pathology. Identifying these index complications may render an in situ marker of patients needing escalation of care. Thus, the aim of this study was to identify which postoperative complications are most strongly associated with death following emergency surgery for GI obstruction or perforation.

Methods

This study was approved by the ethical committee (J.nr. 16-000014) of Zealand Region, Denmark. The requirement for written informed consent was waived by the committee. Approval by the Danish Data Protection Agency (REG-149-2016) and the Danish Patient Safety Authority (3-3013-1999/1) was granted. The manuscript adheres to the Strengthening the Reporting of Observational studies in Epidemiology (STROBE) statement.[15]

All patients scheduled for emergency gastrointestinal surgery between July 1, 2014, and July 31, 2015, at three hospitals in Zealand Region, Denmark, were retrospectively included. The hospitals treat all emergency cases among 800,000 citizens. Emergency treatment is offered free of charge at public hospitals in Denmark, with no private alternative. Emergency surgery is performed day and night without barriers, and extra staff are on call if needed. At the hospitals in our study, general chief surgeons or surgeons in their final year of specialization are on duty around the clock. If the surgeon is still in training, a chief surgeon is on call.

We included patients aged 18 years or older who underwent emergency surgery for GI obstruction or perforation diagnosed by radiological examination. Thus, minor procedures as appendectomies and cholecystectomies were excluded. Emergency surgery was defined as the need for laparoscopy or laparotomy without planned delay. We excluded patients who had undergone intraabdominal surgery up to 30 days prior to the index procedure, patients with an iatrogenic or traumatic perforation, patients pregnant at the time of surgery, or patients receiving chronic dialysis. Patients eligible for inclusion more than once were only included at the first procedure. Only Danish residents were included.

We manually screened all patients planned for GI surgery in the electronic booking system used at the participating hospitals. All emergency procedures due to obstruction or perforation, or undescribed cases were identified through the patients' personal identification number, which allowed data collection from the electronic patient files. Data from the pre-, intra-, and postoperative courses were collected. The postoperative follow-up was 90 days on complications and mortality. Mortality data completeness was achieved through the Danish Civil Registration System. Data were collected between June 15, 2017, and March 31, 2018.

All patient files were accessed by two independent, clinically experienced researchers, and the data collected in two separate case report forms. Case report forms were regularly assessed by the project leader (AWV) to settle disagreements. Minor variations were solved by the project leader. Major inconsistencies were settled through dialogue between the project leader and the senior consultant responsible for the study (BB). Double data entry was performed, and irregularities corrected according to the case report form. Finally, a range check was performed for all data.

The preoperative data collected were age, sex, smoking and alcohol habits, height, weight, comorbidity

(hypertension, cardiac, pulmonary, renal, diabetes, or presence of active cancer), American Society of Anesthesiologists physical status classification (ASA class), Sepsis-2 score, description of the radiological examinations, and time-to-surgery defined as time from decision of surgery to surgery. The intraoperative variables collected were time of surgery, the procedure performed, the intraabdominal pathology, intravenous fluid administration, and blood loss. The postoperative variables collected were Sepsis-2 score, re-admissions, and in-hospital complications as defined in Table 1. Only complications occurring postoperatively were registered and graded according to the Clavien-Dindo Classification.[16] Preoperative conditions were evaluated and only in case of substantial postoperative worsening was the condition registered as a complication (increase in CDC class)[17], e.g., medically treated pneumonia preoperatively was only registered as a complication if it warranted mechanical respiratory support postoperatively. The date of appearance was used for complications.

The primary exposure variables comprised 16 predefined complications (Table 1). We combined some individual complications that are considered to evolve in continuum or had similar treatment profiles. The follow-up on complications was contemplated as 90 days for all complications

Table 1 Definition of postoperative complications

Complication	Variable	Defined by treatment
Superficial wound complication	Superficial wound rupture	Conservative or surgical treatment
	Superficial wound infection	Wound rupture, a need for removal of infected tissue, or medical treatment
Deep wound complication	Deep wound infection and fascial defect	A need for surgical cleavage or removal of infected tissue with fascial defect
	Fascia dehiscence	Spontaneous fascial rupture with a need for re-operation
Peritonitis	Peritonitis	Debut postoperatively
	Intraabdominal abscess	Suspected radiologically and with a need for surgical or medical treatment
Prolonged paralysis	Prolonged paralysis of intestine	≥4 days without defecation
GI bleeding	Gastrointestinal bleeding	A need for surgical or endoscopic treatment
Packed blood products		Transfusion with packed blood, thrombocytes, or plasma
Pneumonia		Diagnosed by the treating physician and medical treatment initiated
Urinary tract infection		Diagnosed by the treating physician and medical treatment initiated
Atrial fibrillation		Verified by electrocardiogram and a need for treatment
Pleural exudation	Exudation to the pleural cavity	Verified by radiology
Pulmonary edema	Pulmonary congestion	With a need for medical treatment
	Pulmonary edema	Radiographic suspicion and a need for intensive care
Respiratory failure	CPAP	A need for non-invasive ventilation or continuous positive airway pressure (CPAP) after the day of extubation
	Failure to wean	Intubation continued for more than 48 h after surgery
	Re-intubation	Re-intubation of any cause
Venous thrombo-embolic event	Deep venous thrombosis	Verified by radiology
	Pulmonary embolism	Verified by scintigraphy or CT scan
Arterial thrombo-embolic event	Acute myocardial infarction	ECG-pathology and treatment initiated
	Stroke	Relevant radiology or diagnosed by a neurologist
	Disseminated intravascular coagulopathy	Diagnosed by the treating physician
Renal impairment	Renal failure	A need for dialysis with or without treatment
	Other renal	Hydronephrosis or nephritis
Re-operation	Superficial wound rupture or infection	With a need for surgical intervention
	Fascial rupture	Spontaneous fascial rupture with a need for intraabdominal surgery
	Separation of stoma	Requiring intraabdominal surgery
	Anastomosis leakage	Requiring intraabdominal surgery
	Re-perforation	Requiring intraabdominal surgery
	Peritonitis or abscess	Requiring intraabdominal surgery
	Postoperative obstruction of intestine	Requiring intraabdominal surgery
	Gastrointestinal bleeding	Intraabdominal surgery pro hemostasis

as most of the complications demanded hospital admission. Planned operations such as a "second-look" or change of vacuum-assisted coverings were not deemed complications. The primary outcome was 90-day all-cause mortality.

Statistics

Parametric and non-parametric statistics were used as appropriate. We presented events of complications as numbers and absolute risks. All-cause mortality was presented as a risk for individual groups of complications (FTR). The primary outcome was analyzed using a multivariable Cox proportional hazards model. To evaluate the influence of the first complication on mortality, we delayed the entry time to the date of the complication; i.e., the patient was included as unexposed (no complication) before that date, thereby avoiding immortal time bias.[18] Any patient who did not die within the predefined 90 days was censored. The model presumes a progressive time span between a complication and death. Some complications appeared on the same day as death. Thus, half a day was added to the day of death or censoring. If a date was missing on a complication, the median time from surgery to the same complication in the cohort was used, or the time to death if it appeared first.

We created a multivariable model adjusting for variables significantly ($p < 0.05$) associated with death in a univariable Cox regression model with delayed entry. All variables demonstrating a significant association were included in the model. Several significant variables were found (Supplementary Tables 1–11), and we decided post hoc to limit the adjusted analysis to complications occurring in over 40 patients to avoid overparameterization. Independent variables in the model were as follows: hospital, age, ASA class (categorized in class 1–2 or 3–5), pre-operative Sepsis-2 score (categorized as group 0–2 or 3–4), cardiac comorbidity (yes or no), hypertension (yes or no), renal comorbidity (yes or no), active cancer (yes or no), the diagnosis (bowel obstruction or perforation), and the type of surgery (bowel resection and stoma formation or other procedures). Three preoperative Sepsis-2 scores were missing. Data on all other independent variables were complete. Post hoc, we decided to replace the missing preoperative Sepsis-2 scores. We used the postoperative Sepsis-2 score and subtracted the median increase in Sepsis-2 score (1.0 (IQR 1.0–2.0)) between the pre- and postoperative course. A test for linearity demonstrated a better fit for age in the potency. Proportionality was tested using Schoenfeld residuals. The proportionality assumption was violated by the variable "active cancer"; hence, the baseline hazard was stratified by the "active cancer" group. We performed subgroup analyses for patients with GI obstruction or perforation. Bonferroni correction was used based on 16 outcomes, and a 2-sided p value of < 0.003 was considered significant. We used R version 3.5.0 GUI 1.70 El Capitan©R Foundation for Statistical Computing, 2016, and RStudio version 1.1.453 for the statistical analysis.

Results

A total of 349 patients were included in the analysis (Fig. 1). The follow-up on complications and death was complete (31,410 patient days) due to the link between the patient files system and the Danish Civil Registration System.[19]

We registered 832 complications during the 90-day follow-up in 281 (80.5%) patients. Patients with a complication were more likely to have a higher ASA class and gastrointestinal perforation (Table 2). Dates were missing for 35 (4.2%) complications (Table 3). The median time to the first appearing complication was 3.0 days (IQR 1–4).

On the day of surgery and the first postoperative day (POD), 105 (12.6%) complications and 19 (20.9%) deaths were registered (Table 3). A total of 420 (50.5%) complications appeared between POD 2 and 7; 211 (25.4%) complications between POD 8 and 30; and 61 (7.3%) complications between POD 31 and 90 (Supplementary Fig. 1). The incidence of complications was evenly distributed between POD 0 and 7 and POD 8 and 90 for deep wound complications (24 vs. 21), renal impairment (12 vs. 11), and re-operations (41 vs. 38). The majority of the following complications appeared late in the postoperative course (POD 0–7 vs. POD 8–90): superficial wound complications (25 vs. 51), peritonitis (8 vs. 16), urinary tract infection (10 vs. 30), pleural exudation (22 vs. 34), and venous thrombo-embolic events (1 vs. 5).

The overall risk of death was 26.1% (91) at 90-day follow-up. The patients who died tended to be older, had a higher ASA class or Sepsis-2 score preoperatively, and more often had known active cancer than surviving patients (Table 2). Further to this, these patients more often had gastrointestinal perforation and anastomosis or stoma formation. Time to surgery was not significantly associated with the risk of complications or death.

Complications and Death

The risk of death was 20.6% (14) for patients with none of the registered complications, and 27.4% (77) for patients with complications. In the group with no registered complications, 13 of the 14 deceased patients increased in Sepsis-2 score after surgery and 10 had septic shock and died within postoperative day one. The risk of death, according to the 16 individual complications (FTR), ranged from 21% in patients with prolonged paralysis to more than 50% for patients with renal impairment or atrial fibrillation (Table 4).

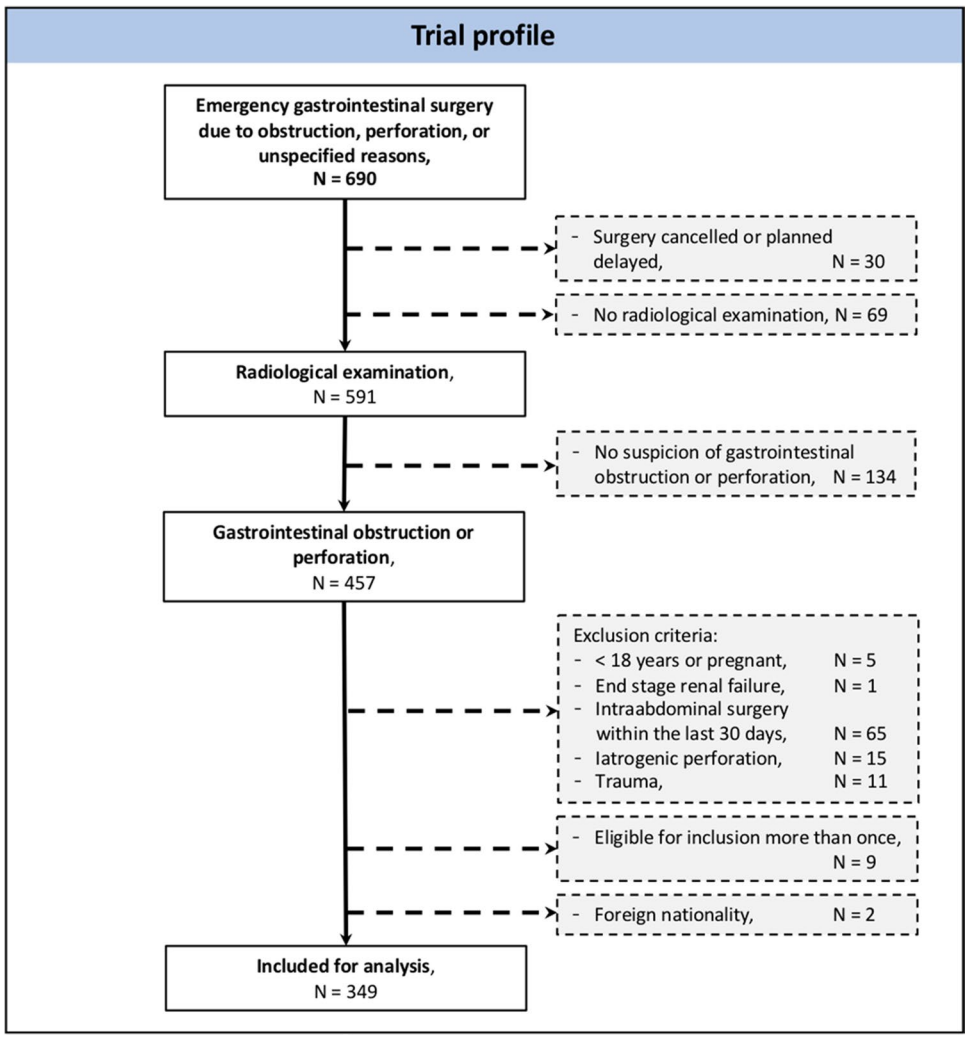

Fig. 1 Trial profile

The crude Cox regression analysis with delayed entry showed that out of ten significant associations, renal impairment, arterial thromboembolic events, and atrial fibrillation were the complications most strongly associated with death (Table 4). The adjusted multivariable model showed 7 significant associations out of 11 analyzed complications. Atrial fibrillation (HR 3.3 (95%CI 2.1–5.2), $p < 0.001$), deep wound complication (HR 3.2 (1.7–5.8), $p < 0.001$), and respiratory failure (HR 2.9 (1.6–5.1), $p < 0.001$) were most strongly associated with 90-day mortality (Table 4).

Out of all patients, 87 (24.9%) had only 1 complication with a mortality risk of 14.9%; 2 complications appeared in 57 (16.3%) patients and the mortality risk was 17.5%; and 3 or more complications appeared in 137 (39.3%) patients with a mortality risk of 39.4% (Supplementary Fig. 1).

Gastrointestinal Obstruction or Perforation

In total, 261 patients had GI obstruction, of whom 204 (78.2%) had 1 or more of 547 registered complications. The overall 90-day mortality risk was 21.8% (57). The risk of death was 15.8% (9) for patients with no complications and 23.5% (48) for patients with complications. Of the nine deceased patients with no registered complications, five had septic shock and died within postoperative day one. The crude Cox regression model demonstrated 10 complications significantly associated with 90-day mortality, of which renal impairment, pulmonary edema, and respiratory failure dominated (Table 5).

Eighty-eight patients had GI perforation, of whom 77 (87.5%) had 1 or more of 285 registered complications. The overall 90-day mortality risk was 38.6% (34). The risk of death was 45% (5) for patients with none of the registered complications and 37.7% (29) for patients with complications. Of the five deceased patients with no registered complications, all had septic shock and died within postoperative day one. Atrial fibrillation was the only complication significantly associated with death in this subgroup of patients. In both subgroups, the number of patients with complications was small, so no adjusted analysis was performed.

Table 2 Background characteristics according to the incidence of complications or death

	Patients with no complication	Patients with a complication	*p* value	Alive at follow-up	Deceased at follow-up	*p* value
Number of patients	68	281		258	91	
Sex, female, no. (%)	40 (58.8)	157 (55.9)	0.76	142 (55.0)	55 (60.4)	0.44
Age, years, median [IQR[φ]]	71.5 [57.8, 79.8]	71.0 [63.0, 79.0]	0.59	69.0 [59.2, 77.0]	77.0 [71.5, 83.0]	< 0.01
BMI[§], median [IQR]	25.0 [20.7, 28.8]	23.9 [21.3, 27.1]	0.35	24.1 [21.3, 28.0]	23.6 [20.8, 26.6]	0.11
Missing, no	8	19		22	5	
Actively smoking, no. (%)	18 (28.6)	95 (34.5)	0.45	87 (35.1)	26 (28.9)	0.35
Missing, no	5	6		10	1	
Excess alcohol intake[#], no. (%)	4 (6.2)	36 (13.3)	0.18	32 (13.0)	8 (9.2)	0.46
Missing, no	4	11		11	4	
ASA class*, no. (%)						
Class 0–2	43 (63.2)	146 (52.0)	0.12	168 (65.1)	21 (23.1)	< 0.01
Class 3–5	25 (36.8)	135 (48.0)	0.12	90 (34.9)	70 (76.9)	< 0.01
Sepsis-2 score, pre-operative, no. (%)						
Group 0–2	42 (61.8)	152 (54.1)	0.65	161 (62.9)	31 (34.4)	< 0.01
Group 3–4	26 (38.2)	129 (45.9)	0.65	95 (37.1)	59 (65.6)	< 0.01
Co-existing diseases, no. (%)						
Cardiac comorbidity	17 (25.0)	81 (28.8)	0.63	64 (24.8)	34 (37.4)	0.03
Hypertension	31 (45.6)	124 (44.1)	0.94	107 (41.5)	48 (52.7)	0.08
Pulmonary comorbidity	10 (14.7)	49 (17.4)	0.72	41 (15.9)	18 (19.8)	0.49
Renal comorbidity	2 (2.9)	26 (9.3)	0.14	13 (5.0)	15 (16.5)	< 0.01
Diabetes mellitus	7 (10.3)	42 (14.9)	0.43	36 (14.0)	13 (14.3)	1.00
Active cancer	11 (16.2)	43 (15.3)	1.00	29 (11.2)	25 (27.5)	< 0.01
Intraabdominal pathology, no. (%)						
Adhesions	34 (50.0)	122 (43.4)	0.40	132 (51.2)	24 (26.4)	< 0.01
Ulcer disease	3 (4.4)	25 (8.9)	0.33	18 (7.0)	10 (11.0)	0.32
Diverticulitis	5 (7.4)	24 (8.5)	0.94	21 (8.1)	8 (8.8)	1.00
Intraabdominal cancer	9 (13.2)	46 (16.4)	0.65	29 (11.2)	26 (28.6)	< 0.01
Hernia	2 (2.9)	12 (4.3)	0.88	10 (3.9)	4 (4.4)	1.00
Crohn disease	3 (4.4)	2 (0.7)	0.08	4 (1.6)	1 (1.1)	1.00
Vascular ischemia	4 (5.9)	5 (1.8)	0.14	5 (1.9)	4 (4.4)	0.38
Volvulus	2 (2.9)	19 (6.8)	0.37	17 (6.6)	4 (4.4)	0.62
Other	6 (8.8)	26 (9.3)	1.00	22 (8.5)	10 (11.0)	0.63
Surgical indication, no. (%)						
GI[¤] obstruction	57 (83.8)	204 (72.6)	0.08	204 (79.1)	57 (62.6)	< 0.01
GI perforation	11 (16.2)	77 (27.4)	0.08	54 (20.9)	34 (37.4)	< 0.01
Time to surgery, h, median [IQR]	4.0 [2.8, 6.0]	3.0 [2.0, 6.0]	0.43	3.0 [2.0, 6.0]	3.0 [2.0, 5.0]	0.63
Intra- and post-operative course						
Surgical access, no. (%)						
Laparoscopy	6 (8.8)	16 (5.7)	0.50	18 (7.0)	4 (4.4)	0.54
Laparotomy	62 (91.2)	265 (94.3)	0.50	240 (93.0)	87 (95.6)	0.54
Surgical procedure, no. (%)						
Other procedure	32 (47.1)	122 (43.4)	0.68	128 (49.6)	26 (28.6)	< 0.01
Bowel resection and stoma formation	36 (52.9)	159 (56.6)	0.68	130 (50.4)	65 (71.4)	< 0.01
Fluid administration, L, median [IQR]	1.8 [1.1, 2.2]	2.1 [1.5, 3.1]	< 0.01	1.9 [1.3, 2.7]	2.3 [1.6, 3.2]	0.02
Missing, no	0	1		0	1	
Blood loss, L, median [IQR]	0.0 [0.0, 0.1]	0.1 [0.0, 0.3]	0.01	0.0 [0.0, 0.3]	0.01 [0.0, 0.3]	0.16

Table 2 (continued)

	Patients with no complication	Patients with a complication	*p* value	Alive at follow-up	Deceased at follow-up	*p* value
Time of surgery, hour, median [IQR]	1.6 [1.0, 2.2]	1.9 [1.4, 2.8]	0.01	1.8 [1.3, 2.6]	2.0 [1.4, 2.9]	0.17
Missing, no	0	7		7	0	
Time at recovery room, hour median [IQR]	3.0 [2.0, 6.0]	6.0 [3.0, 12.0]	< 0.01	5.0 [3.0, 11.0]	6.0 [3.0, 12.0]	0.32
Missing, no	2	3		1	4	

[φ]Inter-quartile range

[§]Body mass index

[#] > 7 drinks/week for women or > 14 drinks/week for men

[*]American Society of Anesthesiologists Classification of physical status

[¤]Gastrointestinal

Discussion

In this observational retrospective study of patients undergoing emergency surgery for gastrointestinal obstruction or perforation, we found that 81% of the patients had complications, 27% of whom were deceased at 90-day follow-up. One-third of the complications debuted after the first week of surgery, and the majority of patients had two or more complications. Renal impairment and arterial thromboembolic events showed the strongest association with death, but were rare. In the adjusted analysis, the complications showing the strongest association with death at 90-day follow-up were atrial fibrillation and deep wound complications.

We found a significant association in 10 of 16 complications and death with varying hazard rates of 2.4–6.8 and risk of death ranging from 32 to 57%. The variability supports our hypothesis that different complications correlate unevenly with death and emphasizes the importance of both minor (e.g., atrial fibrillation) and major (e.g., renal impairment) complications in the postoperative course in the urgent care setting.

The risk of death in patients with complications is known as failure-to-rescue (FTR). When initially introduced by Silber in 1992, the FTR metric included arrhythmia.[10] Alternative definitions followed, some of which focused on surgical complications (e.g., wound infection or re-operations), while others primarily included medical complications (e.g., pulmonary, cardiac, or infectious).[11,20] In contrast to most other studies in the field, which register the most severe complications, our focus in this study was on the first appearance of a specific complication and its association with death. Further to this, we considered the unexposed time (without a complication) and the exposed time (time after the appearance of a complication) to avoid immortal time bias. Interestingly, we found that atrial fibrillation and deep wound complication (fascia dehiscence and deep wound infection) demonstrated the highest hazard ratio for death. Fascia dehiscence was the primary reason for a re-operation in our cohort.

Re-operation was performed in 23% of the patients in our cohort, with mortality risk of 32%, and was strongly associated with death. The association has previously been documented following emergency laparotomy, with a risk of re-operations ranging from 20 to 36%.[4,21,22] However, the mortality risk varies widely, falling between 20 and 72%. Re-operations have been associated with an increased risk of medical complications and additional re-operations, with each additional re-operation increasing the risk of death.[23] Such findings have several possible explanations: the surgical stress response is repeated, an inflammatory response amplified, and the side effects of intravenous fluid therapy and the anaesthesia accumulate and may accelerate an adverse outcome.

Re-operations are generally not optional. Not operating could have vital consequences, and re-operations may be the only chance to rescue the patient. In our study, unplanned re-operations were dominated by fascia dehiscence. We found 11% with fascia dehiscence. The risk of fascia dehiscence varies between 3.8 and 28% following emergency laparotomy[21,24] and is associated with morbidity and death.[25,26] Moreover, the risk of fascia dehiscence is associated with patient- and doctor-related factors. The dominant patient-related factors are obesity, smoking and alcohol habits, or the presence of peritonitis. The iatrogenic factors are choice of suture and sewing technique. One study found that the risk of fascia dehiscence and subsequent death significantly decreased, compared to a historical cohort, following use of a new suture and sewing technique in patients undergoing emergency laparotomy.[25]

A striking finding in our study was the marked association between atrial fibrillation and death. Although we found that different complications dominate in patients with GI obstruction or perforation, atrial fibrillation uniformly demonstrated one of the strongest associations with death in both

Table 3 Number of patients with a complication according to the postoperative day (POD)

Complication	Events/missing dates	POD 0–1	POD 2–7	POD 8–14	POD 15–30	POD 31–90
		Patients with a complication, no. (%)				
Superficial wound complication	81 / 5	5 (6.2)	20 (24.7)	22 (27.2)	22 (27.2)	7 (8.6)
Superficial wound rupture	43					
Superficial wound infection	38					
Deep wound complication	45 / 0	1 (2.2)	23 (51.1)	16 (35.6)	4 (8.9)	1 (2.2)
Deep wound infection	5					
Fascia dehiscence	40					
Peritonitis	24 / 0	0 (0.0)	8 (33.3)	8 (33.3)	7 (29.2)	1 (4.2)
Peritonitis	4					
Intraabdominal abscess	20					
Prolonged paralysis	145 / 0	-	145 (100.0)	-	-	-
Gastrointestinal bleeding	19 / 0	5 (26.3)	6 (31.6)	4 (21.1)	2 (10.5)	2 (10.5)
Packed blood products	47 / 6	12 (25.5)	24 (51.1)	3 (6.4)	2 (4.3)	0 (0.0)
Pneumonia	110 / 6	21 (19.1)	48 (43.6)	21 (19.1)	8 (7.3)	6 (5.5)
Urinary tract infection	44 / 4	3 (6.8)	7 (15.9)	6 (13.6)	12 (27.3)	12 (27.3)
Atrial fibrillation	63 / 4	28 (43.8)	25 (39.1)	3 (4.7)	1 (1.6)	2 (3.2)
Pleural exudation	62 / 6	4 (6.5)	18 (29.0)	21 (33.9)	6 (9.7)	7 (11.3)
Pulmonary edema	53 / 4	10 (18.9)	26 (49.1)	6 (11.3)	4 (7.5)	3 (5.7)
Pulmonary congestion	41					
Pulmonary edema	12					
Respiratory failure	63 / 0	7 (11.1)	42 (66.7)	11 (17.5)	2 (3.2)	1 (1.6)
CPAP[¤]	24					
Failure to wean (> 48 h)	21					
Re-intubation	18					
Venous TEE[Φ]	6 / 0	0 (0,0)	1 (16.7)	2 (33.3)	0 (0.0)	3 (50.0)
Deep venous thrombosis	2					
Pulmonary embolus	4					
Arterial TEE	17 / 0	3 (17.6)	7 (41.2)	2 (11.8)	1 (5.9)	4 (23.5)
Acute myocardial infarction	9					
Stroke	4					
DIC*	3					
Arterial thrombosis	1					
Renal impairment	23 / 0	3 (13.0)	9 (39.1)	2 (8.7)	3 (13.0)	6 (26.1)
Renal failure	8					
Other renal	15					
Re-operation	79 / 0	4 (5.1)	37 (46.8)	25 (31.6)	6 (7.6)	7 (8.9)
Superficial wound rupture	9					
Deep wound rupture	37					
Anastomotic leakage	2					
Separation of stoma	1					
Re-perforation	6					
Peritonitis or abscess	2					
Post-operative obstruction	21					
Laparotomy pro hemostasis	1					
Death	91 / 0	19 (20.9)	9 (9.9)	14 (15.4)	15 (16.5)	34 (37.4)

[¤]Continuous positive airway pressure

[Φ]Thrombo-embolic events

[*]Disseminated intravascular coagulation

Table 4 Risk of a complication or all-cause mortality at 90 days and their association

	Risk of a complication	Death (FTR[§])	Crude analysis		Adjusted analysis[θ]	
	No. (%)	No. (%)	HR (95% CI) [#]	*p*	HR (95% CI)	*p*
Superficial wound complication	81 (24)	20 (25)	1.7 (1.0–2.9)	0.0393	1.6 (0.9–2.7)	0.1204
Deep wound complication*	45 (13)	16 (36)	2.5 (1.4–4.4)	0.0015	3.2 (1.7–5.8)	0.0001
Peritonitis	24 (7)	9 (38)	2.6 (1.3–5.4)	0.0067	-	-
Prolonged paralysis	145 (43)	30 (21)	1.1 (0.7–1.7)	0.8060	1.3 (0.8–2.2)	0.2872
Gastrointestinal bleeding	19 (6)	7 (37)	2.8 (1.3–6.2)	0.0084	-	-
Packed blood-products	47 (14)	21 (45)	3.1 (1.9–5.2)	< 0.0001	1.7 (1.0–2.9)	0.0643
Pneumonia	110 (32)	40 (36)	3.4 (2.2–5.3)	< 0.0001	2.4 (1.5–3.8)	0.0003
Urinary tract infection	44 (13)	11 (25)	2.0 (1.0–3.8)	0.0376	1.7 (0.8–3.4)	0.1494
Atrial fibrillation	63 (19)	33 (52)	4.4 (2.8–6.8)	< 0.0001	3.3 (2.1–5.2)	< 0.0001
Pleural exudation	62 (18)	26 (42)	3.9 (2.4–6.4)	< 0.0001	2.3 (1.4–4.0)	0.0019
Pulmonary edema	53 (16)	25 (47)	4.0 (2.5–6.4)	< 0.0001	2.3 (1.4–3.8)	0.0011
Respiratory failure	63 (18)	29 (43)	3.9 (2.4–6.2)	< 0.0001	2.9 (1.6–5.1)	0.0003
Venous TEE[Φ]	6 (2)	2 (33)	2.6 (0.6–10.6)	0.1840	-	-
Arterial TEE[Φ]	17 (5)	8 (47)	4.8 (2.3–9.9)	< 0.0001	-	-
Renal impairment	23 (7)	13 (57)	6.8 (3.7–12.4)	< 0.0001	-	-
Re-operation	79 (23)	25 (32)	2.4 (1.5–3.9)	0.0006	2.7 (1.6–4.5)	0.0001

[§]Failure-to-rescue

[#]Hazard ratio (95% confidence interval)

[θ]Variables adjusted for in the multivariable analysis: Hospital (Holbæk, Slagelse, and Køge), age, ASA class (categorized in class 1–2 or 3–5), pre-operative sepsis-2 score (categorized in group 0–2 or 3–4), cardiac comorbidity (yes or no), hypertension (yes or no), renal comorbidity (yes or no), active cancer (yes or no), the diagnosis (bowel obstruction or perforation), and the type of surgery (bowel resection and stoma formation or other procedures)

*Analyzed for laparotomies only, excluding 22 laparoscopic procedures

ΦThrombo-embolic events. A p value < 0.003 is considered significant

subgroups of patients. Atrial fibrillation is the most common postoperative arrhythmia. The incidence varies according to the type of surgery, ranging from 1.4% in non-cardiac surgery to over 30% following cardiac surgery. [27,28] The risk of atrial fibrillation in our cohort was 19%.

The association between atrial fibrillation and a postoperative adverse course has been documented following esophagostomies and cardiac surgery, but studies within gastrointestinal surgery are scarce.[29–31] Postoperative atrial fibrillation has previously been associated with sepsis, a leaking bowel anastomosis, or death,[31–34] which supports our finding. The pathophysiological relation is, however, not well understood, since it is unlikely that atrial fibrillation alone is the mediator of various complications or death. The inflammatory response and release of catecholamines following surgery have been argued to prompt postoperative atrial fibrillation. The association between atrial fibrillation and stroke or myocardial infarction has been documented and is a rational relation.[35] However, the association between atrial fibrillation and subsequent surgical complications is more difficult to explain. It has been argued that atrial fibrillation alters circulation and may compromise blood flow at the surgical site. Another possible explanation is that perioperative intravenous fluid administration combined with a hormonal stress response that prompts fluid retention causes tissue edema and also induces atrial fibrillation; this further accelerates the risk of pulmonary congestion and edema of the surgical site and thus poor wound and anastomosis healing.[36] Both mechanisms may explain why atrial fibrillation appears early in the postoperative course, whereas surgical complications evolve days to weeks later. Our results suggest that postoperative onset of atrial fibrillation should prompt a thorough assessment of the patient to detect underlying pathology and may serve as an early marker of patients needing escalation of care.

The strengths of our study are the double data extraction and registration, clear definitions of study variables, and the analytical adjustment for delayed entry to avoid immortal time bias.[18] The contribution from multiple sites increases the external validity and generalizability of the study results.

The limitations of our study are inherent in the retrospective design that relies on patient files. We compensated for this by using clear definitions of complications and conducting double registration of the prospectively collected data in a public health system ensuring 100% follow-up on mortality of all Danish residents.[19] Despite

Table 5 The association between complications and 90-day mortality was stratified on subgroups with gastrointestinal obstruction or perforation

	Gastrointestinal obstruction				Gastrointestinal perforation			
			Crude analysis				Crude analysis	
	Risk of a complication, no. (%)	Death (FTR[§]), no. (%)	Hazard ratio (95% CI[#])	*p*	Risk of a complication, No. (%)	Death (FTR[§]), no. (%)	Hazard ratio (95% CI[#])	*p*
Superficial wound complication	56 (21)	10 (18)	1.2 (0.6–2.5)	0.5610	25 (28)	10 (40)	2.9 (1.2–7.0)	0.0173
Deep wound complication*	32 (12)	10 (31)	2.3 (1.1–4.7)	0.0193	13 (15)	6 (46)	2.5 (0.9–6.8)	0.0678
Peritonitis	11 (4)	6 (55)	4.7 (2.0–11.0)	0.0004	13 (15)	3 (23)	1.0 (0.3–3.3)	0.9740
Prolonged paralysis	103 (39)	18 (17)	1.0 (0.5–1.8)	0.9240	42 (48)	12 (29)	1.1 (0.5–2.6)	0.8590
GI[¤] bleeding	13 (5)	5 (38)	3.3 (1.3–8.3)	0.0115	6 (7)	2 (33)	-	-
Packed blood-products	29 (11)	13 (45)	3.2 (1.7–6.1)	0.0002	18 (20)	8 (44)	2.6 (1.1–5.9)	0.0271
Pneumonia	75 (29)	27 (36)	3.9 (2.3–6.8)	< 0.0001	35 (40)	13 (37)	2.3 (1.0–4.9)	0.0386
Urinary tract infection	35 (13)	10 (29)	2.5 (1.3–5.2)	0.0093	9 (10)	1 (11)	-	-
Atrial fibrillation	41 (16)	20 (49)	4.6 (2.6–7.9)	< 0.0001	22 (25)	13 (59)	3.4 (1.7–6.8)	0.0008
Pleural exudation	34 (13)	15 (44)	4.5 (2.5–8.3)	< 0.0001	28 (32)	11 (39)	2.7 (1.2–6.4)	0.0210
Pulmonary edema	29 (11)	16 (55)	5.7 (3.2–10.3)	< 0.0001	24 (27)	9 (38)	1.8 (0.8–4.2)	0.1410
Respiratory failure	41 (16)	18 (44)	5.2 (2.9–9.1)	< 0.0001	27 (31)	11 (41)	2.1 (0.9–4.8)	0.0841
Venous TEE[Φ]	4 (2)	2 (50)	-	-	2 (2)	0 (0)	-	-
Arterial TEE[Φ]	10 (4)	5 (50)	4.8 (1.9–12.1)	0.0009	7 (8)	3 (43)	-	-
Renal impairment	17 (7)	10 (59)	9.5 (4.7–19.0)	< 0.0001	6 (7)	3 (50)	-	-
Re-operation	55 (21)	16 (29)	2.6 (1.4–4.7)	0.0024	24 (27)	9 (38)	1.7 (0.7–4.0)	0.2050

[§]Failure-to-rescue

[#]Confidence interval

[¤]Gastrointestinal

[*]Analyzed for laparotomies only, excluding 22 laparoscopic procedures

[Φ]Thrombo-embolic events. A *p* value < 0.003 is considered significant

a clear definition of the cohort, different intraabdominal pathologies were disclosed and could have unevenly influenced the risk of complications and death. However, we corrected for important confounders in the adjusted analysis. No matter the adjustment, the results of this study are merely hypothesis-generating.

Our study discloses a particularly vulnerable group of patients and an eventful postoperative course following emergency gastrointestinal surgery. The intraabdominal pathology involved every segment of the GI tract, and a variety of surgical interventions were performed. Future studies are encouraged to address how these variables may influence the association between specific complications and death. Importantly, the associations we found between renal impairment, arterial thrombosis, or atrial fibrillation and death were strong and should be addressed in future trials to test for causality. Another area to address in future studies is the marked risk of death (21%) within the first day after surgery.

Conclusion

In this observational study of patients undergoing emergency surgery for gastrointestinal obstruction or perforation, we found that 80% of the patients had a complication and that two-thirds of the complications appeared within the first postoperative week. Renal impairment and arterial thromboembolic events, though rare, showed the strongest association with death. Of the more frequent complications, atrial fibrillation and deep wound complications were most strongly associated with death. Atrial fibrillation was uniformly associated with death in both subgroups of patients with gastrointestinal obstruction or perforation and may serve as an important early marker of patients needing escalation of care.

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Author Contribution AWV: Developed the idea, obtained legislative and ethical approvals, planned the study, searched the literature, drafted the protocol, collected the data, planned the analysis and interpretation, conducted the analysis, drafted the present manuscript, revised and approved the final manuscript, and raised the funds.

AAA, JB, and SE: Collected the data, revised the analysis and interpretation, and revised and approved the final manuscript.

AWB, RL, SJ, and HE: Collected the data, interpreted the data, and revised and approved the final manuscript.

LCT and AMM: Planned the study, refined the drafted protocol, planned the analysis, revised the analysis and interpretation, and revised and approved the final manuscript.

BB: Planned the study, refined the drafted protocol, planned the analysis, revised the analysis and interpretation, revised and approved the final manuscript, responsible for initiating and conducting the trial, raised the funds.

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Declarations

Ethics Standards This study was approved by the ethical committee (J.nr. 16-000014) of Zealand Region, Denmark.

Consent to Participate The requirement for written informed consent was waived by the committee.

Consent to Publication All the authors have approved the manuscript and agree to its submission.

Conflict of Interest The authors declare no competing interests.

References

1. Saunders DI, Murray D, Pichel AC, Varley S, Peden CJ, UK Emergency Laparotomy Network. Variations in mortality after emergency laparotomy: the first report of the UK Emergency Laparotomy Network. *Br J Anaesth*. 2012;109(3):368–375. https://doi.org/10.1093/bja/aes165
2. Barrow E, Anderson ID, Varley S, et al. Current UK practice in emergency laparotomy. *Ann R Coll Surg Engl*. 2013;95(8):599-603. https://doi.org/10.1308/rcsann.2013.95.8.599
3. Symons NRA, Moorthy K, Almoudaris AM, et al. Mortality in high-risk emergency general surgical admissions. *Br J Surg*. 2013;100(10):1318-1325. https://doi.org/10.1002/bjs.9208
4. Iversen LH, Bülow S, Christensen IJ, Laurberg S, Harling H. Postoperative medical complications are the main cause of early death after emergency surgery for colonic cancer. *Br J Surg*. 2008;95:1012-1019. https://doi.org/10.1002/bjs.6114
5. Simões CM, Carmona MJC, Hajjar LA, et al. Predictors of major complications after elective abdominal surgery in cancer patients. *BMC Anesthesiol*. 2018;18(1):49. https://doi.org/10.1186/s12871-018-0516-6
6. Pearse RM, Moreno RP, Bauer P, et al. Mortality after surgery in Europe: a 7 day cohort study. *Lancet*. 2012;380(9847):1059-1065. https://doi.org/10.1016/S0140-6736(12)61148-9
7. McCoy CC, Englum BR, Keenan JE, Vaslef SN, Shapiro ML, Scarborough JE. Impact of specific postoperative complications on the outcomes of emergency general surgery patients. *J Trauma Acute Care Surg*. 2015;78(5):912-919. https://doi.org/10.1097/TA.0000000000000611
8. Khuri SF, Henderson WG, DePalma RG, et al. Determinants of long-term survival after major surgery and the adverse effect of postoperative complications. *Ann Surg*. 2005;242(3):326–341; discussion 341–3. https://doi.org/10.1097/01.sla.0000179621.33268.83
9. Tengberg LT, Cihoric M, Foss NB, et al. Complications after emergency laparotomy beyond the immediate postoperative period - a retrospective, observational cohort study of 1139 patients. *Anaesthesia*. 2017;72(3):309-316. https://doi.org/10.1111/anae.13721
10. Silber JH, Williams S V., Krakauer H, Schwartz JS. Hospital and patient characteristics associatedwith death after surgery: a study of adverse occurrence and failure to rescue. *Med Care*. 1992;30(7):615-627. https://doi.org/10.1097/00005650-199207000-00004
11. Holena DN, Kaufman EJ, Delgado MK, et al. A metric of our own: failure to rescue after trauma. *J Trauma Acute Care Surg*. 2017;83(4):698-704. https://doi.org/10.1097/TA.0000000000001591
12. Metcalfe D, Castillo-Angeles M, Olufajo OA, et al. Failure to rescue and disparities in emergency general surgery. *J Surg Res*. 2018;231:62-68. https://doi.org/10.1016/j.jss.2018.04.047
13. Mehta A, Efron DT, Canner JK, et al. Effect of surgeon and hospital volume on emergency general surgery outcomes. *J Am Coll Surg*. 2017;225(5):666-675.e2. https://doi.org/10.1016/j.jamcollsurg.2017.08.009
14. Ghaferi AA, Birkmeyer JD, Dimick JB. Complications, failure to rescue, and mortality with major inpatient surgery in medicare patients. *Ann Surg*. 2009;250(6):1029-1033. https://doi.org/10.1097/SLA.0b013e3181bef697
15. Elm E von, Altman DG, Egger M, et al. Strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. *BMJ*. 2007;335(7624):806-808. https://doi.org/10.1136/bmj.39335.541782.AD
16. Dindo D, Demartines N, Clavien P-A. Classification of surgical complications. *Ann Surg*. 2004;240(2):205-213. https://doi.org/10.1097/01.sla.0000133083.54934.ae
17. Mentula PJ, Leppäniemi AK. Applicability of the Clavien-Dindo classification to emergency surgical procedures: a retrospective cohort study on 444 consecutive patients. *Patient Saf Surg*. 2014;8(1):31. https://doi.org/10.1186/1754-9493-8-31
18. Hanley JA, Foster BJ. Avoiding blunders involving "immortal time." *Int J Epidemiol*. 2014;43(3):949-961. https://doi.org/10.1093/ije/dyu105
19. Pedersen CB. The Danish Civil Registration System. *Scand J Public Health*. 2011;39(7_suppl):22–25. https://doi.org/10.1177/1403494810387965
20. Johnston MJ, Arora S, King D, et al. A systematic review to identify the factors that affect failure to rescue and escalation of care in surgery. *Surgery*. 2015;157(4):752-763. https://doi.org/10.1016/j.surg.2014.10.017
21. Kim JJ, Liang MK, Subramanian A, Balentine CJ, Sansgiry S, Awad SS. Predictors of relaparotomy after nontrauma emergency general surgery with initial fascial closure. *Am J Surg*. 2011;202(5):549-552. https://doi.org/10.1016/j.amjsurg.2011.06.023
22. Kassahun WT, Mehdorn M, Wagner TC. The effects of reoperation on surgical outcomes following surgery for major abdominal emergencies. A retrospective cohort study. *Int J Surg*. 2019;72:235–240. https://doi.org/10.1016/j.ijsu.2019.11.024

23. Martínez-Casas I, Sancho JJ, Nve E, Pons MJ, Membrilla E, Grande L. Preoperative risk factors for mortality after relaparotomy: analysis of 254 patients. *Langenbeck's Arch Surg*. 2010;395(5):527-534. https://doi.org/10.1007/s00423-009-0538-0
24. Marwah S, Marwah N, Singh M, Kapoor A, Karwasra RK. Addition of rectus sheath relaxation incisions to emergency midline laparotomy for peritonitis to prevent fascial dehiscence. *World J Surg*. 2005;29(2):235-239. https://doi.org/10.1007/s00268-004-7538-6
25. Tolstrup M-B, Watt SK, Gögenur I. Reduced rate of dehiscence after implementation of a standardized fascial closure technique in patients undergoing emergency laparotomy. *Ann Surg*. 2017;265(4):821-826. https://doi.org/10.1097/SLA.0000000000001762
26. van Ramshorst GH, Eker HH, van der Voet JA, Jeekel J, Lange JF. Long-term outcome study in patients with abdominal wound dehiscence: a comparative study on quality of life, body image, and incisional hernia. *J Gastrointest Surg*. 2013;17(8):1477-1484. https://doi.org/10.1007/s11605-013-2233-2
27. Gialdini G, Nearing K, Bhave PD, et al. Perioperative atrial fibrillation and the long-term risk of ischemic stroke. *JAMA - J Am Med Assoc*. 2014;312(6):616-622. https://doi.org/10.1001/jama.2014.9143
28. Maesen B, Nijs J, Maessen J, Allessie M, Schotten U. Post-operative atrial fibrillation: a maze of mechanisms. *Europace*. 2012;14(2):159-174. https://doi.org/10.1093/europace/eur208
29. Schizas D, Kosmopoulos M, Giannopoulos S, et al. Meta-analysis of risk factors and complications associated with atrial fibrillation after oesophagectomy. *Br J Surg*. 2019;106(5):534-547. https://doi.org/10.1002/bjs.11128
30. Lomivorotov V V., Efremov SM, Pokushalov EA, Karaskov AM. New-onset atrial fibrillation after cardiac surgery: pathophysiology, prophylaxis, and treatment. *J Cardiothorac Vasc Anesth*. 2016;30(1):200-216. https://doi.org/10.1053/j.jvca.2015.08.003
31. Walsh SR, Oates JE, Anderson JA, Blair SD, Makin CA, Walsh CJ. Postoperative arrhythmias in colorectal surgical patients: incidence and clinical correlates. *Color Dis*. 2006;8(3):212-216. https://doi.org/10.1111/j.1463-1318.2005.00881.x
32. Bhave PD, Goldman LE, Vittinghoff E, Maselli J, Auerbach A. Incidence, predictors, and outcomes associated with postoperative atrial fibrillation after major noncardiac surgery. *Am Heart J*. 2012;164(6):918-924. https://doi.org/10.1016/j.ahj.2012.09.004
33. Wells CI, Robertson JP, Campbell S, Al-Herz F, Rhind B, Young M. Impact of atrial fibrillation on long-term survival following oesophagectomy: a 21-year observational study. *ANZ J Surg*. 2018;88(4):E268-E272. https://doi.org/10.1111/ans.14054
34. Siu CW, Tung HM, Chu KW, Jim MH, Lau CP, Tse HF. Prevalence and predictors of new-onset atrial fibrillation after elective surgery for colorectal cancer. *PACE - Pacing Clin Electrophysiol*. 2005;28(SUPPL. 1). https://doi.org/10.1111/j.1540-8159.2005.00024.x
35. AlTurki A, Marafi M, Proietti R, et al. Major adverse cardiovascular events associated with postoperative atrial fibrillation after noncardiac surgery a systematic review and meta-analysis. *Circ Arrhythmia Electrophysiol*. 2020;13(1):71-80. https://doi.org/10.1161/CIRCEP.119.007437
36. Marjanovic G, Villain C, Juettner E, et al. Impact of different crystalloid volume regimes on intestinal anastomotic stability. *Ann Surg*. 2009;249(2):181-185. https://doi.org/10.1097/SLA.0b013e31818b73dc