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Postoperative arrhythmia after lower gastrointestinal surgery- the blind spot of postoperative care?

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Abstract

Introduction: Postoperative arrhythmias (PAs) are common events and have been widely investigated in cardiothoracic surgery. Within visceral surgery, a recent study revealed a significant occurrence of PA in esophageal resections. In contrast, PA in lower gastrointestinal surgery is rarely investigated and has been rudimentary described in the medical literature.

Methods: In total, 1171 patients (559 female, 612 male) without any history of prior arrhythmia who underwent lower GI surgery between 2012 and 2018 were included and retrospectively analyzed. All included patients were treated and monitored in the intensive care unit (ICU) or intermediate care unit (IMC) after surgery. Follow-up was obtained for the patients with PA investigating the possible persistence of PA and complications such as permanent arrhythmia or thromboembolic events after discharge.

Results: Overall, PA occurred in n=56 (4.8%) patients after surgery of the lower GI. The highest incidence of PA was seen in patients undergoing bowel surgery after mesenteric ischaemia (26.92%), followed by cytoreductive surgery (CRS) combined with hyperthermic intraperitoneal chemotherapy (HIPEC; 16.67%). PA was significantly associated with higher age ($p<0.001$) and longer length of stay in the ICU ($p<0.001$). PA was independently associated with organ failure ($p<0.001$) and higher in-house mortality ($p<0.001$). In median, PA occurred 66.5 hours after surgery. In follow-up, 31% of the patients showed development of permanent arrhythmia.

Discussion: The incidence of PA after lower GI surgery is comparatively low. Its occurrence, however, seems to have severe implications since it is significantly associated with higher rates of organ failure and in-house mortality. Also, compared to the general population, the development of permanent arrhythmia is significantly higher in patients who developed new-onset PA.

Introduction

New-onset postoperative arrhythmias (PAs), such as postoperative atrial fibrillation (POAF), represent common and severe events in the perioperative setting after cardiac surgery. Here, the incidence of POAF varies between 20% and 50%.[1,2] For general and visceral surgery, the incidence and impact of PA has not been well described. The existing literature focusses mostly on surgical procedures of the oesophagus with incidence rates ranging from 9–23%.[3–7]. While the incidence of PA in patients undergoing esophagectomies might also be explained by the thoracic part of this surgery, systemic factors such as imbalance of electrolytes, activation of sympathetic system and hypoxia followed by vasoconstriction of pulmonary veins have also been depicted as relevant pathophysiological factors for the genesis of PA.[8]

In a recent study of our group we evaluated the impact of PA in patients after upper GI surgery including not only esophagectomies but also gastrectomies and pancreatectomies[9]. The analysis shows increased in-house-mortality associated significantly with PA (among other findings).

Now, in the present retrospective study our aim was to fade out surgical procedures causing mechanical manipulation on pericardium, myocardium or nerve fibres of the thoracic vagus nerve causing a potential bias for an increased occurrence of PA perioperatively. Therefore our focus here is on patients undergoing surgery of lower GI. For this group of patients previous analysis of the occurrence of PA and its impact are rare: A few studies show incidences ranging from 4.4 to 13.7%.[10–12] To evaluate the impact of PA we also performed long-term follow-ups of patients who underwent lower GI surgery and developed PA regarding possible complications of PA, such as permanent arrhythmias or thromboembolic events.

Methods

Patient cohort

Altogether, 1458 patients who underwent surgery of the lower gastrointestinal (GI) tract at the Department of General, Visceral, and Paediatric Surgery of the University Medical Centre Goettingen, Germany between 2012 and 2018 were screened by retrospective chart analysis. Due to pre-existing arrhythmia or a prior implanted pacemaker in the patient history, n = 287 (19.7%) patients were excluded from further analysis in this study. A total of 1171 patients (559 female, 612 male) were eventually included in this analysis. All included patients were postoperatively treated and monitored at either the intensive care unit (ICU) or intermediate care unit (IMC). Our study was approved by the local ethics committee of the University Medical Centre Goettingen (UMG; study number: 14/2/19). The ethics committee waived the need for informed consent. All experiments were performed in accordance with relevant guidelines and regulations.

Surgical procedures were grouped according to the anatomical localization or type of surgery/indication as following: small bowel resections, ileocecal resections, (extended) right hemicolectomies and resections of the transverse colon, (extended) left hemicolectomies and resections of the sigmoid colon, (sub)total colectomies and proctocolectomies, anterior rectal resections and Hartmann´s procedures, resection rectopexies, low anterior rectal resections, abdominoperineal rectal resections or exenterations, bowel resections after mesenteric ischaemia, multivisceral resections, and cytoreductive surgery (CRS) combined with hyperthermal intraperitoneal chemotherapy (HIPEC).

Among the existing patient data we screened for pre-existing conditions and perioperative complications as multiple cardiovascular risk factors, surgical complications, anastomosis and stump insufficiency, wound healing deficit, Chylus / pancreatic /biliary fistula, revision surgery, postoperative myocardial infarction, organ failure, electrolyte disorders, postoperative deep vein thrombosis, infections, sepsis and usage of beta blocker in premedication (for blood pressure regulation).

Long-term follow-up was obtained from patients who developed PA to screen for permanent arrhythmia, thromboembolic events and overall survival (OS). A standardized questionnaire was used by contacting patients and their general practitioners or cardiologists to ascertain these parameters (Supplementary Fig. 1 shows the translated version of the German questionnaire).

Statistical analysis

Comparisons were performed using the Mann–Whitney U test for continuous variables and the chi-square test or Fisher´s exact test for categorical variables.

A predictive model was developed using multivariate logistic regression analysis to confirm the independent associations between postoperative surgical complications and the occurrence of PA. Preselected surgical complications were set as independent variables, while the occurrence of PA was set as a dependable variable. In another second multivariate logistic analysis, surgical complications were again set as independent variables, while in-house mortality was set as the dependent variable. Odds ratios (ORs) are presented with 95% confidence intervals.

The selection of surgical complications as predictors for these models was realized by single tests in advance.

As 56 patients developed PA, the number of independent variables for the logistic regression was limited to rounded 6 (56/10 = 5.6). All selected variables met the following conditions: significant association with the occurrence of PA ($p < 0.05$) and case number in each group ≥ 15.

Analogous to this, the number of independent variables in the second multivariate logistic regression model was set to 3 (10% of 30), as 30 patients died during hospitalization. All selected variables met the following conditions: significant association with the occurrence of death during hospitalization ($p < 0.05$) and case number in each group ≥ 10.

Statistical analysis was performed using R software (ver. 4.0.2.; R Foundation for Statistical Computing, Vienna, Austria). The global significance level was set to $\alpha = 5\%$.

Results

1. Collection of patients

In total, 1171 patients were enrolled in our retrospective analysis. Surgical procedures included n = 26 cases of mesenteric ischaemia, n = 18 CRS combined with simultaneous HIPEC, n = 185 (extended) right hemicolectomies/resections of the transverse colon, n = 35 (sub)total colectomies/proctocolectomies, n = 92 multivisceral resections, n = 91 abdominoperineal rectal resections/exenterations, n = 418 (extended) left hemicolectomies/sigmoid resections/anterior rectal resections/Hartmann´s procedures, n = 216 low anterior rectal resections, n = 65 ileocecal resections, n = 8 resections of the small bowel, and n = 17 resection rectopexies.

Overall, n = 348 patients (29.7%) showed pre-existing cardiovascular diseases and consecutive perioperative risk factors, such as hypertension, diabetes, coronary heart disease, heart failure, valvular

heart disease, peripheral artery occlusive disease, myocardial infarction or coagulopathies. An overview of all demographic and clinical data is provided in Table 1.

Table 1
Demographic and clinical data of all enrolled patients

parameter	level	total	male	female
n		1171	612	559
Age	mean ± sd	64 ± 14	63 ± 13	63 ± 15
	median (min; max)	65 (18; 96)	64 (18; 96)	65 (18; 95)
Malign diagnosis				
	No	468 (40.0%)	231 (37.7%)	237 (42.4%)
	Yes	703 (60.0%)	381 (62.3%)	322 (57.6%)
Surgery				
	Surgery for mesenteric ischaemia	26 (2.2%)	16 (2.6%)	10 (1.8%)
	HIPEC in multivisceral resection	18 (1.5%)	6 (1.0%)	12 (2.1%)
	(Extended) right hemicolectomy, transverse colon resection	185 (15.8%)	89 (14.5%)	96 (17.2%)
	(Sub-)total colectomy, proctocolectomy	35 (3.0%)	17 (2.8%)	18 (3.2%)
	Multivisceral resections	92 (7.9%)	34 (5.6%)	58 (10.4%)
	Rectal extirpation/exenteration	91 (7.8%)	57 (9.3%)	34 (6.1%)
	(Extended) left hemicolectomy, sigma resection, anterior rectal resection, Hartmann's procedure	418 (35.7%)	217 (35.5%)	201 (36.0%)
	Low anterior rectal resection	216 (18.4%)	140 (22.9%)	76 (13.6%)
	Ileocecal resection	65 (5.6%)	32 (5.2%)	33 (5.9%)
	Small bowel resection	8 (0.7%)	3 (0.5%)	5 (0.9%)
	Resection rectopexy	17 (1.5%)	1 (0.2%)	16 (2.9%)
Hypertension				

parameter	level	total	male	female
	No	546 (46.6%)	280 (45.8%)	266 (47.6%)
	Yes	625 (53.4%)	332 (54.2%)	293 (52.4%)
Diabetes mellitus				
	No	974 (83.1%)	494 (80.7%)	480 (85.9%)
	Yes (Type I/II)	140 (11.2%)	85 (13.9%)	55 (9.8%)
	Metabolic syndrome	57 (4.7%)	33 (5.4%)	24 (4.3%)
Venous thrombosis				
(preoperative)	No	1104 (94.3%)	584 (95.4%)	520 (93.0%)
	Yes	67 (5.7%)	28 (4.6%)	39 (7.0%)
Coronary heart disease				
	No	1036 (88.5%)	516 (84.3%)	520 (93.0%)
	Yes	135 (11.5%)	96 (15.7%)	39 (7.0%)
Embolic event				
	No	1088 (93.0%)	559 (91.5%)	529 (94.6%)
	Yes	82 (7.0%)	52 (8.5%)	30 (5.4%)
Myocardial infarction (preoperative)				
	No	1104 (94.3%)	558 (91.2%)	546 (97.6%)
	Yes	67 (5.7%)	54 (8.8%)	13 (5.4%)
Heart failure				

parameter	level	total	male	female
	No	1121 (95.7%)	579 (94.6%)	542 (97.0%)
	Yes	50 (4.3%)	33 (5.4%)	17 (3.0%)
Valvular heart disease				
	No	1114 (95.1%)	584 (95.4%)	530 (94.8%)
	Yes	57 (4.9%)	28 (4.6%)	29 (5.2%)
Coagulopathies				
	No	1152 (98.4%)	607 (99.2%)	545 (97.5%)
	Yes	19 (1.6%)	5 (0.8%)	14 (2.5%)
Multiple cardiovascular diseases (≥ 2)				
	No	814 (69.5%)	398 (65.0%)	416 (74.4%)
	Yes	357 (30.5%)	214 (35.0%)	143 (25.6%)
Performed cardiac treatment				
	No	1066 (91.0%)	533 (87.1%)	533 (95.3%)
	Yes	105 (9.0%)	79 (12.9%)	26 (4.7%)
Premedication				
	Anticoagulants	299 (25.5%)	184 (30.1%)	115 (20.6%)
	Antiarrhythmics	355 (30.3%)	188 (30.7%)	167 (29.9%)
	Diuretics	316 (27.0%)	165 (27.0%)	151 (27.0%)
	Ras-inhibitors	474 (40.5%)	259 (42.3%)	215 (38.5%)

parameter	level	total	male	female
	Oral antidiabetics	137 (11.7%)	96 (15.7%)	41 (7.3%)
Chirurgical complications intraoperative				
	No	1094 (93.5%)	570 (93.3%)	524 (93.7%)
	Yes	76 (6.5%)	41 (6.7%)	35 (6.3%)
Anastomosis-/ stump insufficiency				
	No	1071 (91.5%)	550 (90.0%)	521 (93.2%)
	Yes	99 (8.5%)	61 (10.0%)	38 (6.8%)
Wound healing deficit/ burst abdomen				
	No	910 (77.8%)	469 (76.8%)	441 (78.9%)
	Yes	260 (22.2%)	142 (23.2%)	118 (21.1%)
Chyle/ pancreatic fistula, bile leakage				
	No	1132 (96.8%)	588 (96.2%)	544 (97.3%)
	Yes	38 (3.2%)	23 (3.8%)	15 (2.7%)
Myocardial infarction (postoperative)				
	No	1167 (99.7%)	608 (99.5%)	559 (100.0%)
	Yes	3 (0.3%)	3 (0.5%)	0 (0.0%)
Revision surgery				

parameter	level	total	male	female
	No	990 (84.6%)	517 (84.6%)	473 (84.6%)
	Yes	180 (15.4%)	94 (15.4%)	86 (15.4%)
Organic failure				
	No	1100 (94.0%)	572 (93.6%)	528 (94.5%)
	Yes	70 (6.0%)	39 (6.4%)	31 (5.5%)
Electrolyte disorders				
	No	911 (77.9%)	489 (80.0%)	422 (75.5%)
	Yes	259 (22.1%)	122 (20.0%)	137 (24.5%)
Thrombosis				
(postoperative)				
	No	1155 (98.7%)	605 (99.0%)	550 (98.4%)
	Yes	15 (1.3%)	6 (1.0%)	9 (1.6%)
Infections				
	No	1014 (86.7%)	516 (84.5%)	498 (89.1%)
	Yes	156 (13.3%)	95 (15.5%)	61 (10.9%)
Sepsis				
	No	1104 (94.4%)	577 (94.4%)	527 (94.3%)
	Yes	66 (5.6%)	34 (5.6%)	32 (5.7%)

2. Incidence of PA

After undergoing surgery of lower GI new-onset PA was seen in n = 56 patients (4.8%), of whom some patients partly developed several types arrhythmias. Detected arrhythmias included bradycardic atrial fibrillation (n = 3), normofrequent atrial fibrillation (n = 3), tachycardic atrial fibrillation (n = 42), atrial

flutter (n = 2), second-degree and third-degree atrioventricular block (n = 3), pulseless electrical activity (n = 2), asystole (n = 5), ventricular fibrillation (n = 1), ventricular tachycardia (n = 1), and arrhythmia with cardiopulmonal resuscitation (n = 1).

In our study, the occurrence of PA was very heterogeneous regarding the different types of abdominal surgery.

The highest incidence of PA was seen in mesenteric ischaemia (26.92%), followed by CRS and HIPEC (16.67%) and (extended) right hemicolectomies/resections of the transverse colon (5.95%). Furthermore, POAF occurred in 5.71% of (sub)total colectomies/proctocolectomies and in 5.43% of multivisceral resections.

The incidence of PA was 4.4% in abdominoperineal rectal resections/exenterations and 3.83% in (extended) left hemicolectomies/sigmoid resections/anterior rectal resections and Hartmann´s procedures. PA emerged in 3.24% of low anterior rectal resections and 1.54% of ileocecal resections. In our cohort of patients, PA was not seen in resections of the small bowel (0%) or resection rectopexies (0%). All surgical procedures and their percentages of arrhythmias are illustrated in Fig. 1.

The median time span between surgery and occurrence of PA was 66.5 hours (mean: 144.59; see Fig. 2A).

3. Risk constellations of developing PA

Our study showed a significant association between the occurrence of PA and age of the patients. The mean age in the PA group was 69.77 years versus 63.56 years in the non-PA group ($p < 0.001$, see Fig. 2B). The strongest predictor for the development of PA using multiple testing was organic failure ($p < 0.001$, odds ratio (OR) = 4.72), followed by revision surgery ($p = 0.08$, OR = 1.89), sepsis ($p < 0.001$, OR = 1.84) and multiple preexisting cardiovascular diseases ($p = 0.07$, OR = 1.57; see Fig. 2C). Supplementary Table 1 shows all variables that are part of the logistic regression model for the development of postoperative arrhythmias with their Odds ratios, p-values and 95% confidence interval.

4. PA and its short-term impact

Patients who suffered from PA had a significantly longer stay in the ICU or IMC (19.02 days versus 4.727 days; $p < 0.001$; see Fig. 2D). Furthermore, the occurrence of PA was significantly associated with increased postoperative in-house mortality as a independent variable in the logistic regression model (16.07% vs. 1.88%; $p < 0.001$, OR: 3.37). Other significantly associated variables for in-house-mortality were infections ($p < 0.05$; OR = 3.89) and sepsis as the strongest predictor ($p < 0.001$; OR = 27.63; see Fig. 3). Supplementary Table 2 is a presentation of the variables that are part of the logistic regression model for in-house mortality with their Odds ratios, p-values and 95% confidence interval.

5. PA and its long-term impact

For n = 56 patients with newly diagnosed PA follow-up was performed as described above. In n = 36 cases sufficient and reliable follow-up data could be obtained. Among those n = 11 patients (31%) had developed paroxysmal or permanent arrhythmia after discharge. Regarding survival analysis, there was no significant difference in OS between patients who developed paroxysmal/permanent arrhythmia (62.56 months) and those who did not (40.65 months; p = 0.2; see Fig. 4).

Discussion

In the existing literature incidence of new-onset PA after lower GI surgery was reported between 4.4% and 13.7% [10 11 12]. Kazaure et al. [13] did a database query of 46,716 patients and showed an incidence of atrial fibrillation (AF) of 5.7% after general surgery in patients aged ≥ 55 years. In the present study our result of the analysis of n = 1171 patients showed an incidence of 4.8%, which is in line with the existing data. Although the incidence is comparably low (compared to cardiothoracic surgery or surgery of upper GI), it might have serious consequences: New-onset PA was significantly associated with prolonged stay on ICU and increased in-house mortality.

The aetiology of new-onset PA is unclear and presumably multifactorial. In upper GI surgery, specifically in oesophageal resection with an incidence between 16.5% and 23.1%[4–7], mechanical manipulation of the myocardium or pericardium is discussed as an important factor. Our previous analysis which investigated the occurrence of PA in patients who underwent upper GI surgery revealed a general incidence of 8.3%[9]. In lower GI surgery different factors are supposed to trigger PA such as an increase in hormonal and sympathetic activity. It results as a stress response due to anaesthesia and surgery [14,15]. Furthermore, surgical trauma and the extent of surgery are suspected to generate postoperative inflammatory processes. For interleukin 6 and 8 that are known to be proinflammatory cytokines, Wu et al. demonstrated an increased expression in peritoneal fluid after colon surgery[16]. Additionally, the finding that PA was correlated to sepsis or infection may underline the hypothesis of an infection associated cause of PA. However, if the inflammatory process is the cause of PA cannot be addressed in this retrospective study. Importantly, the strong association of PA to an increased in-house mortality should highlight its appearance after surgery as a relevant risk factor.

Concerning the time point of the development of PA in our study, the median occurrence of PA was 66.5 hours (mean: 144.59 hours) after surgery, which is in concordance with a previous analysis claiming a peak of arrhythmias within the first four days postoperatively [12,17]. The wide range of occurrence may further strengthen the inflammatory association rather than the fact of a strong correlation to surgery as inflammatory processes may also started later during the hospital stay. Furthermore, this time frame could lead to the assumption that potential arrhythmias of patients being discharged from ICU or IMC treatment in the early postoperative phase (postoperative days 1 (POD 1) and 2 (POD2)) might remain undetected at a normal ward where there is no continuous monitoring. The vast majority of our patients who underwent lower GI surgery were transferred to a normal ward earlier than 66.5 hours after surgery.

Therefore, we assume that the number of unreported events of PA in the perioperative setting is considerably higher.

Regarding the distribution of arrhythmias in our study, the highest incidence was found in mesenteric ischaemia (26.92%). As mesenteric ischaemia mostly occurs due to other pre-existing diseases, particularly because of diverse arteriosclerotic risk factors, many of those patients are expected to suffer from severe heart and vessel diseases.[18,19]. Furthermore, electrolyte imbalances, increased lactate and an increased inflow of inflammatory cytokines occur due to manipulation during surgery. These factors severely impact the occurrence of PA. Interestingly, CRS combined with simultaneous application of HIPEC (16.67%) showed a high percentage of PA. In general, CRS and simultaneous HIPEC include surgery that takes several hours followed by 90 minutes of hyperthermic (42°C/107.6°F) chemotherapy diluted in sodium chloride 0.9%. The duration of this surgery as well as the fact that a volume of up to 5 to 7 litres of diluted chemotherapy passes both the abdominal cave and the oesophageal hiatus entering the mediastinum might have an effect on the development of PA.

In our analysis, when comparing the incidence of PA after right-side hemicolectomy to abdominoperineal rectal resections / exenterations, with the latter causing presumably a significantly larger surgical trauma, the incidence of PA after right-side hemicolectomy was slightly higher (5.95% vs. 4.4%). Therefore, other factors than the pure surgical trauma have to be taken into account. Most likely age and co-morbidities may play a pivotal role explaining the difference. Additionally, the individual risk of each patient respecting their medical histories is another predisposition for the risk of PA [20–22].

In this study, the occurrence of PA was associated with a higher rate of development of permanent/paroxysmal arrhythmia: 31% of all patients who developed PA showed paroxysmal or permanent arrhythmia after discharge, whereas the incidence of AF in a study with an age-matched population is 0.8%.[23]

However, overall survival did not significantly differ between those patients who developed paroxysmal or permanent arrhythmia after PA and those who did not. We believe that this might be blurred by the relevance of other factors such oncological prognosis.

The presented study has certain limitations: The retrospective origin of the analysis does not allow any conclusion about the causalities. Also, the sequence of PA and the appearance of surgical and non-surgical complications have not been documented. Plus, the real incidence of PA after lower GI surgery might be higher because patients generally leave ICU or IMC treatment on the first days after surgery. Hence, a prospective study with close monitoring of patients during the first week after surgery would be of great importance. Additionally, cardiological follow-up after discharge of patients with PA would be desirable. Nevertheless, to the best of our knowledge, this study includes the largest cohort to date detecting the occurrence of PA in patients who underwent lower GI surgery and clearly demonstrated PA as an important risk factor for prolonged ICU stay, increased in-house mortality after surgery and higher risk for development of paroxysmal/permanent arrhythmia after discharge.

Declarations

Data availability

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Author contributions

F.R. contributed to the design of the study, to the analysis of clinical data and the manuscript preparation. M.S.H. contributed to the acquisition of the data. D.E. contributed to the acquisition of the data as well as to the statistical analysis. A.F.M. contributed to the acquisition of the data. T.T. contributed to the design of the study and the critical revision of the manuscript. A.L. contributed to the statistical analysis of the data. M.B. contributed to the acquisition of the data and the critical revision of the manuscript. M.G. contributed to the design of the study and the critical revision of the manuscript. T.P. contributed to the design of the study as well as to the critical revision of the manuscript. A.A. contributed to the design of the study, to the data acquisition as well as to the critical revision of the manuscript. J.G. contributed to the design of the study, to the interpretation of clinical data as well as to the drafting of the manuscript.

Data availability statement

Drs Rühlmann and Azizian had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Additional Information

The authors declare that they have no competing conflict of interest.

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Figures

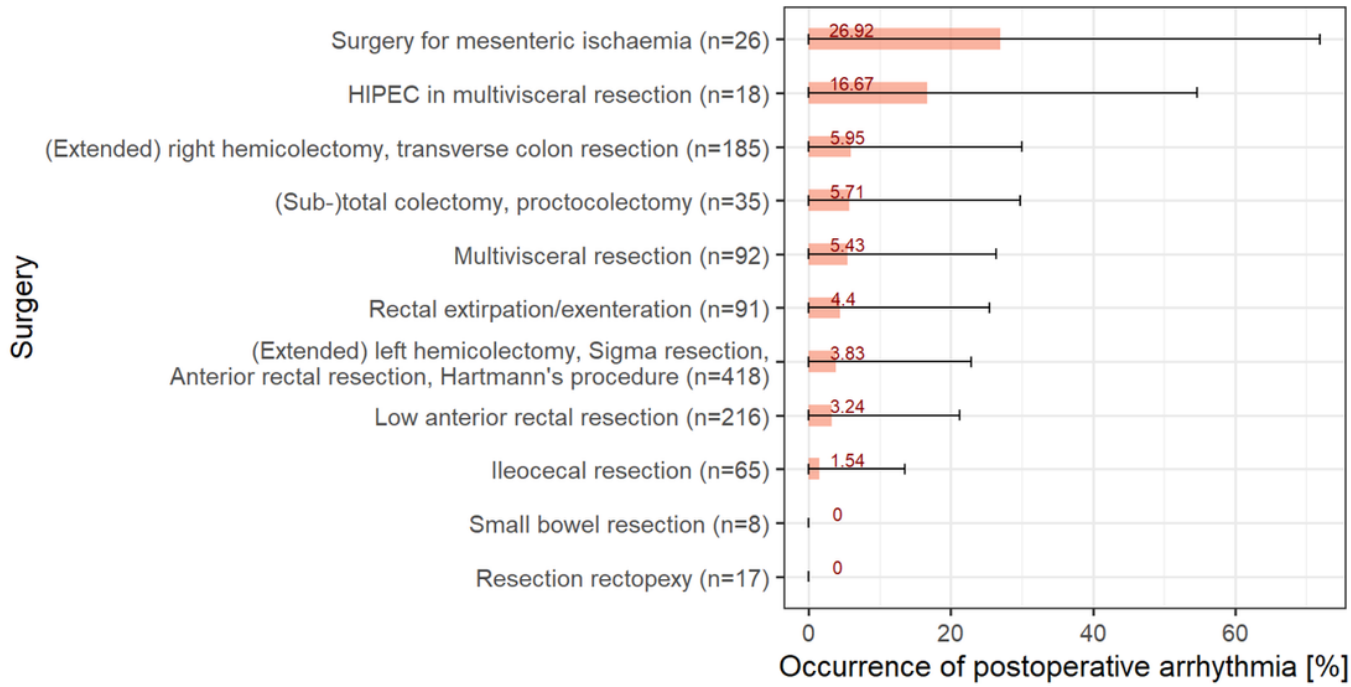

Figure 1

Incidence and distribution of postoperative arrhythmia in different types of lower gastrointestinal surgery. Error bars represent the +1 standard deviation.

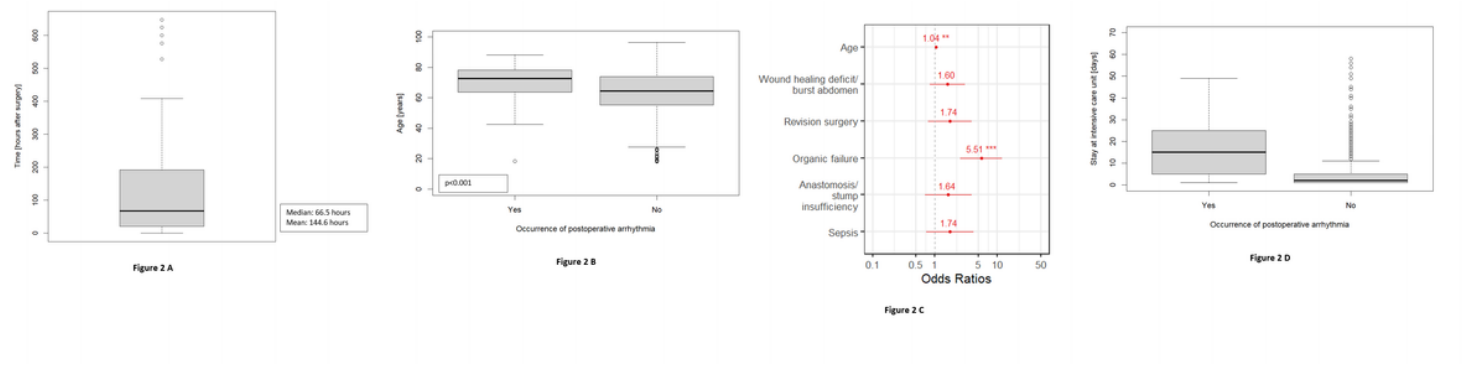

Figure 2

A: Time span between surgery and the occurrence of PA.

B: Distribution of age in years in the cohorts of patients with and without PA.

C: Variables associated with PA as part of the logistic regression model with their Odds ratios, p-values (*= <0.05, **= <0.01, ***= <0.001) and 95% confidence interval.

D: Distribution of stay on Intensive Care Unit (ICU) in days in the cohorts of patients with and without PA

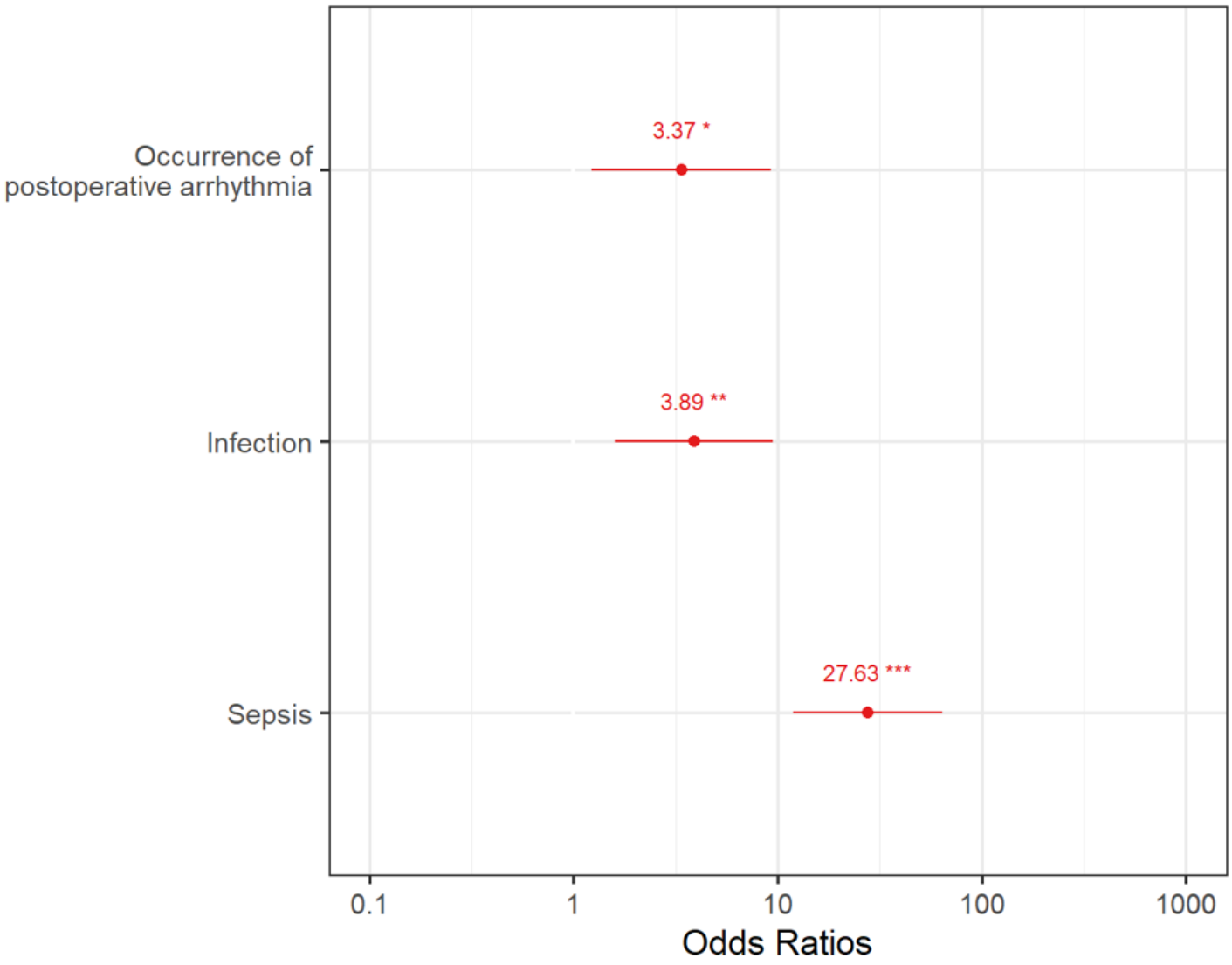

Figure 3

Variables that are part of the logistic regression model for the in-house-mortality during inpatient length of stay with their Odds ratios, p-values (*= <0.05, **= <0.01, ***= <0.001)

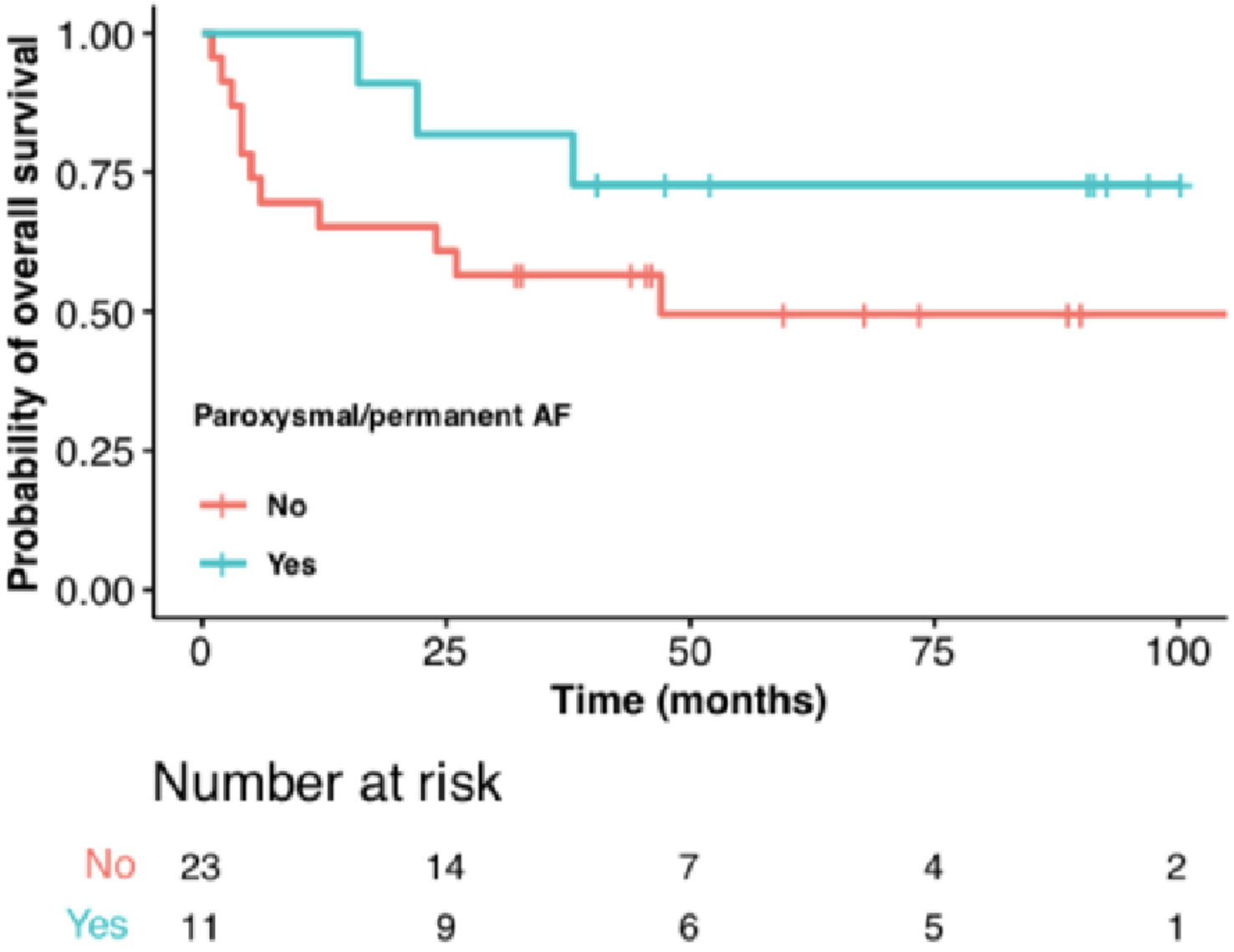

Figure 4

Kaplan-Meier-Curve of patients who developed paroxysmal/permanent PA (blue) and those who did not develop paroxysmal/permanent PA (red). No significant difference in overall survival was obtained.

Supplementary Files

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- SupplFigure1.doc