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Original Article

Effects of left ventricular ejection fraction on morbidity and mortality in major abdominal surgery

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Abstract: Objective: Our aim in this study was to investigate the effects of Left Ventricular Ejection Fraction (LVEF) on the clinical results of patients who underwent major abdominal procedures due to the malignancies of the gastrointestinal system (GIS). Methods: GIS malignancy procedures, which were electively performed in our clinic between 2013 and 2016, were included in the study. The patients were divided into 4 groups according to their LVEF and were classified as < 30% (Group 1), 30% to 44% (Group 2), 45% to 54% (Group 3) and > 55% (Group 4). Subgroup analysis was performed among the patients with and without peroperative events. In subgroup analysis, independent risk factors were determined using logistic regression analysis for peroperative events in patients undergoing surgery for GI malignancy. Results: A total of 220 patients were covered by the study, including 12 patients in Group 1, 13 patients in Group 2, 25 patients in Group 3, and 170 patients in Group 4. When Group 1 was evaluated, it was seen that 91.7% of the patients had a score of ASA 3 and 58.7% of the patients were on index 4 according to Lee's Revised Cardiac Risk Index. No significant differences were observed among the groups with regards to preoperative laboratory results, BMI, and pulmonary function test values. No differences were found among the groups regarding diagnoses at the time of admission, surgical procedures performed, duration of operation, and blood transfusion during operation as well. Moreover, there were no significant differences between surgical or non-surgical postoperative complications and the mortality cases within 30 days after surgery. Mortality was seen in three patients and all these patients had an LVEF value higher than 44%. The subgroup multivariate analysis of perioperative complications revealed that diabetes mellitus (DM) (p: 0.017, OR: 2.457, CI: 0.194-0.853), duration of operation over 300 minutes (p: 0.001, OR: 2.68, CI: 0.204-0.682) and older than 65 years (p: 0.007, OR: 2.341, CI: 0.230-0.794) were independent risk factors. Conclusion: When assessed according to LVEF, there was no difference between groups in terms of morbidity and mortality according to Clavian Dindo Classification. We believe that major abdominal procedures for GIS malignancies with low LVEF can be performed with acceptable morbidity and mortality rates at experienced centers.

Keywords: Non-cardiac surgery, low ejection fraction, mortality, morbidity, abdominal surgery

Introduction

Non-cardiac surgical procedures pose a significant risk for mortality and morbidity in patients with cardiovascular disease or cardiovascular disease risk factors. Cardiac complications can be seen in patients with documented or asymptomatic ischemic heart disease (IHD), left ventricular (LV) dysfunction, valvular heart disease (VHD) and arrhythmia, and prolonged hemodynamic and cardiac stress related procedures [1]. Moreover, the risk of developing complications is closely related to the preoperative medical condition of the patient, the presence of comorbidities, and other factors associated with surgical procedures [2].

There is a limited number of studies which have demonstrated the effects of LVEF on complications following abdominal surgery [1, 3]. In their study, Rohde *et al*. found out that EF < 30% was an independent risk factor for complications in non-cardiac surgeons [3]. The average age and the size of patient population with GIS malignancies requiring surgical intervention has been growing day by day, and related to this, indi-

viduals with cardiovascular diseases have been more frequently on the agenda of clinicians. In this study, we aimed to investigate the effects of LVEF on postoperative morbidity and mortality in patients undergoing major abdominal surgery due to GIS malignancy in our clinic.

Left ventricular dysfunction is a significant factor affecting hospital mortality and morbidity. Our aim in this study was to investigate the effects of LVEF on the clinical results of patients who underwent major abdominal procedures due to the malignancies of the GIS.

Methods

Study design

This is a retrospective observational study conducted at a tertiary training and research hospital. Following the approval of the Clinical Research Evaluation Board of Kartal Kosuyolu Higher Specialization Training and Research Hospital (Registration No: 2016.5/1-12), patients who underwent surgery having been diagnosed with GIS malignancy in our clinic were included in the study. It was not necessary to have the patients' informed consents because of the retrospective nature of the study.

Study population

Inclusion criteria: Cases of major abdominal surgery performed in our hospital because of GIS malignancy under elective conditions between January 2013 and December 2016. Exclusion criteria: Patients who underwent surgery under emergency conditions with no oncologic surgery and who had missing file records.

LVEF evaluation and grouping

Transthoracic ecocardiographic evaluation was performed by Vingmed System Five GE ultrasonography machine (Horten, Norway) with 2.5 MHz probe on left lateral position. LV end-diastolic diameter, LV end-systolic diameter, interventricular septum thickness, and posterior wall thickness on parasternal long axis images were measured. The ejection fraction was calculated from these values according to the modified Simpson method.

The patients were allocated to 4 groups based on their LVEF according to the reference limits and values recommended by the American Society of Echocardiography (ASE) [4]. Those with LVEF < 30% were classified as severely abnormal (Group 1), those with 30% to 44% as moderately abnormal (Group 2), those with 45% to 54% as mildly abnormal (Group 3) and those with > 55% as normal (Group 4).

Data

The age, gender, comorbidities, admission diagnosis, body mass index, LVEF, respiratory function parameters (FEV1, FVC), laboratory test results, Lee's Revised Cardiac Risk Index, and the American Society of Anesthesiologists (ASA) Clustering data of the patients included in the study were recorded pre-operatively.

Surgical procedures, intraoperative blood transfusion requirements, duration of operation and hospitalization, morbidity and mortality rates were recorded as well. Post-operative mortality cases during the first 30 days follow-up period were evaluated as operative mortality while surgical complications developed during this period were considered to be morbidity.

All the data were saved in Excel tables without any identifying information to prevent patients' names from being revealed.

The primary endpoint of the study: To investigate the effects of LVEF on morbidity and mortality in patients undergoing major abdominal surgery due to GIS malignancy.

The secondary endpoint of the study: To investigate the risk factors for peroperative complications in patients undergoing major abdominal surgery due to GIS malignancy.

Statistical analysis

Statistical software package (SPSS 21 Inc., Chicago, IL, USA) was used for biostatistical analyses. The data obtained from the patients participating in the study were expressed as mean, standard deviation values and in percentages where appropriate. The distribution of the data was checked by the Kolmogorov-Simirnov test. The ANOVA test was used for the comparison of multiple groups with normally distributed data and the Student T test was used for binary group comparisons. Nonpara-

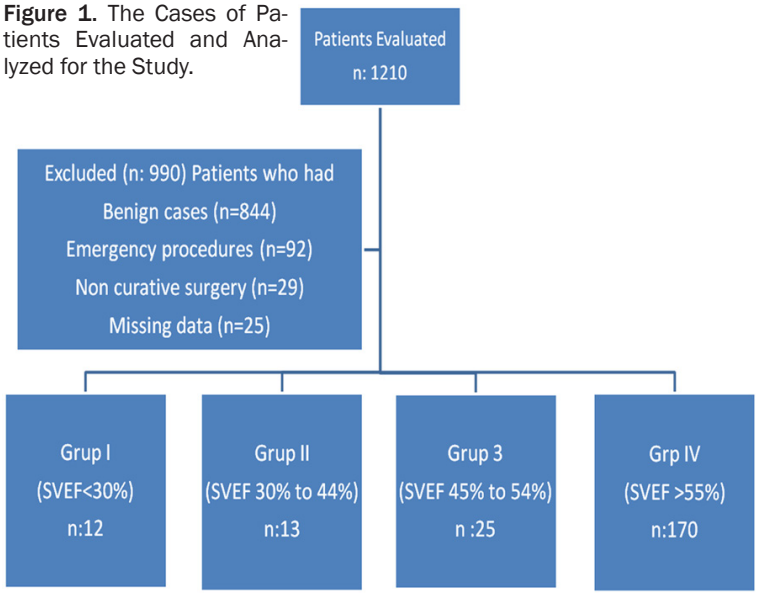

Figure 1. The Cases of Patients Evaluated and Analyzed for the Study.

metric data were analyzed by the Kruskal-Wallis analysis in multiple group comparisons while the Mann-Whitney U test was utilized in binary group comparisons. Categorical groups were compared by the Chi-Square test. In the subgroup analysis of the postoperative complication, univariate logistic regression analysis of each variable was performed as the first step in the establishment of the multivariable logistic regression model in order to determine the candidate variables to enter the model. If the probability value of the Wald test statistics was less than the determined error level of 0.25 ($p < 0.25$), the relevant variables were included in the multivariate model. The odds ratio, 95% confidence interval of the results were calculated and statistical significance was set at the $p < 0.05$ level.

Results

The cases of a total of 1210 patients who underwent surgery in our clinic between January 2013 and December 2016 were reviewed. A total of 990 cases, which had emergency surgery (n = 92), surgery due to benign diseases (n = 844), malignant cases without curative surgery (n = 29), and those with missing file data (n = 25), were excluded from the study (**Figure 1**). There were 12 patients in Group 1 with severe abnormality (< 30%) according to LVEF, 13 patients in Group 2 with moderate abnormality (30% to 44%), 25 patients in Group 3 with mild abnormality (45% to 54%), and 170 patients in Group 4 who were within normal bounds (> 55%).

When comorbidities and medical histories of the patients were evaluated, it was seen that coronary artery disease and previous history of coronary artery bypass graft (CABG) procedures were significantly higher in Group 1 and 2 than the other groups ($p = 0.01$). There was a statistically significant difference among the groups in ASA and Lee's Revised Cardiac Risk Index scores performed as pre-surgical risk assessment ($p = 0.01$). When Group 1 was analyzed, it was observed that 91.7% of the patients were ASA 3 and 58.7% of the patients' Lee's Revised Cardiac Risk Index was 4. There were no significant differences among the groups in terms of preoperative laboratory results, BMI, and respiratory function test values. The clinical characteristics of the patients have been summarized in **Table 1**.

When the operation diagnoses were examined, it was seen that 81 patients had been diagnosed with stomach cancer, 63 with colon cancer, 43 with rectal cancer, and 33 with other malignancies (esophagus, pancreas, primary or metastatic hepatic tumors). No statistically significant difference was found among the groups when the surgical procedures and the admission diagnoses were explored. The duration of surgical procedures and the intraoperative blood transfusion showed no difference among the groups. The diagnoses, surgical procedures performed, and intraoperative findings have been summarized in **Table 2**.

There was no statistically significant difference among the groups with regards to surgical or non-surgical postoperative complications and mortality rates within 30 days following surgery. Three patients had mortality and all of these patients had LVEF above 44%. These patients were secondarily lost because of multiorgan failure due to anastomotic leaks. Although the duration of hospitalization was found to be higher in Group 3 with 15.8±10.4 days than the

Table 1. Baseline Characteristics of Patients Undergoing Major Abdominal Malign Surgery

Variable		Group 1	Group 2	Group 3	Group 4	*P*-value
Age (median.sd)		63±11.3	64.3±1.1	66.4±10.9	60.5±11.5	0.078
Sex n (%)	Male	9 (75%)	8 (61.5%)	17 (68%)	104 (61.2%)	0.740
	Famale	3 (25%)	5 (38.5%)	8 (32%)	66 (38.8%)	
Laboratory	Hemotocrit	35.2±4.2	35.8±5.33	36.7±5.56	35.5±5.22	0.75
	Albumin (g/dl)	4±0.3	3.8±0.50	3.9±0.4	3.9±0.5	0.563
	Creatinin (mg/dl)	1.08±0.66	1.18±0.72	0.85±0.35	0.86±0.36	0.181
Comorbidities n (%)	DM	3 (25%)	4 (30.8%)	9 (36%)	32 (17.6%)	0.210
	COPD	4 (33.3%)	4 (30.8%)	5 (20%)	14 (8.2%)	0.05
	CRF	1 (8.3%)	2 (15.4%)	1 (4%)	2 (1.2%)	0.12
	CAD	10 (80%)	7 (53.8%)	10 (40%)	16 (9.4%)	0.01*
	HT	5 (41.7%)	4 (30.8%)	10 (40%)	44 (25.9%)	0.357
	History of stroke	1 (8.3%)	1 (7.7%)	1 (4%)	3 (1.7%)	0.337
	CABG	5 (41.7%)	3 (23.1%)	2 (8%)	7 (4.1%)	0.01*
History of tobacco use n (%)		3 (25%)	6 (46.2%)	9 (36%)	59 (34.7%)	0.740
ASA	1	0	0	2 (8%)	49 (28.8%)	0.01*
	2	0	1 (7.7%)	5 (20%)	69 (40.6%)	
	3	11 (91.7%)	12 (92.3%)	18 (72%)	92 (41.8%)	
	4	1 (8.3%)	0	0	1 (0.6%)	
Lee Revised Cardiac Risk Index	1	0	0	0	0	0.01*
	2	1 (8.3%)	5 (38.5%)	16 (64%)	144 (75.5%)	
	3	4 (33.3%)	7 (53.8%)	8 (32%)	25 (14.7%)	
	4	7 (58.3%)	1 (7.7%)	1 (4%)	1 (0.6%)	
BMI (kg/m^2)		28.1±3.7	26.8±4.09	29.05±5.39	27.6±4.4	0.419
Pulmonary function tests	FVC	96±18	86±21	92±9	98±16	0.076
	FEV1	95±19	80±24	90±14	94±16	0.077

Group 1, EF < 30%; Group 2, EF 30% to 44%; Group 3, EF 45% to 54%; Group 4, EF > 55%; DM, Diabetes Mellitus; COPD, chronic obstructive pulmonary disease; CRF, Chronic renal failure; CAD, Coronary artery disease; HT, Hypertensıon; CABG, Coronary Arter Bypass Greft; LEVF, Leftventricul ejection fraction; BMİ, Body mass index; FVC, Forced expiratory vital capacity; FEV1, Forced Expiratory Volume in the first second; ASA, American Society of Anesthesiologists; NYHA, New York Heart Association.
*Differences between the groups with Chi-square test is statistically significant p < 0.05.

other groups, there was no statistically significant difference among the groups. Comparisons of postoperative complications according to the Clavian-Dindo Classification and follow-up findings have been summarized in **Table 3**.

When the cases of patients, who developed perioperative morbidity and mortality and those who were discharged without any complications, were compared through univariate logistic regression test, it was seen that differences regarding DM, age (≥ 65), BMI (≥ 25), and duration of operation (≥ 300 min) between the two groups were significantly higher in the patient group with post-operative complications (**Table 4**).

The results of the analysis, performed as a consequence of the univariant logistic regression analysis among the variables fit for multivariate logistic regression, revealed that age (≥ 65) (OR: 2.341, 95% CI 0.230 to 0.794 p = 0.07), DM (OR: 2.457, 95% CI 0.194 to 0.853, p = 0.017), and duration of operation (≥ 300 min) (OR: 2.68, 95% CI 0.204 to 0.682, p = 0.001) were statistically significant (**Table 5**). When model fit was examined by the Hosmer-Lemeshow test, it was concluded that the model was a sufficient one (Chi-square: 2.567 df: 8 and p = 0.959).

Discussion

Various risk indices have been defined to determine perioperative cardiac risk for about the last thirty years. Goldman *et al.* [5] defined, for the first time in 1977, a cardiac risk index for patients scheduled for orthopedic, urological, and general surgery. The current Lee's index,

Table 2. Surgıcal Procedure Type and Intraoperative Findings

Variable		Group 1	Group 2	Group 3	Group 4	*P*-value
Diagnosis	Gastric Cancer	2 (2.5%)	4 (4.9%)	7 (8.6%)	68 (84%)	0.592
	Colon Cancer	4 (6.3%)	3 (4.8%)	8 (12.7%)	48 (76.2%)	
	Rectum Cancer	3 (7%)	5 (11.6%)	5 (11.6%)	30 (69.8%)	
	Other	3 (9.1%)	1 (3%)	5 (15.2%)	24 (72.7%)	
Surgical Procedures	TG + D2 LND	1 (3.1%)	3 (9.4%)	4 (12.5%)	24 (75%)	0.942
	DSG + D2 LND	1 (2%)	1 (2%)	3 (6.1%)	44 (89.8%)	
	Right Hemicolectomy	2 (12.5%)	1 (6.3%)	2 (12.5%)	11 (68.8%)	
	Left Hemicolectomy	1 (7.7%)	1 (7.7%)	3 (23.1%)	8 (61.5%)	
	Anterior Resection	1 (2.9%)	1 (2.9%)	3 (8.8%)	29 (85.3%)	
	LAR + İleostomy	1 (6.3%)	2 (12.5%)	2 (12.5%)	11 (68.8%)	
	LAR	2 (7.4%)	3 (11.1%)	3 (11.1%)	19 (70.4%)	
	Other Surgical Procedures	3 (9.1%)	1 (3%)	5 (15.2%)	24 (75%)	
Surgical duration (minute)	< 300	10 (83.3%)	112 (84.6%)	17 (68%)	97 (57.1%)	0.066
	≥ 300	2 (16.7%)	2 (12.5%)	8 (32%)	73 (42.9%)	
Intraoperative blood transfusion	Yes	3 (25%)	2 (15.5%)	4 (16%)	22 (12.9%)	0.692
	No	9 (75%)	11 (84.6%)	21 (84%)	148 (87.1%)	

Group 1, EF < 30%; Group 2, EF 30% to 44%; Group 3, EF 45% to 54%; Group 4, EF > 55%; Other, eusophagus, pancreas, primary or metastatic liver tumors, TG, total gastrectomy; D2 LND, d2 lymph node dissection; LAR, low anterior resection.

Table 3. Postoperative follow-up and complications

Variable		Group 1	Group 2	Group 3	Group 4	*P*-value
No complication		7 (58.3%)	9 (69.2%)	11 (44%)	102 (60%)	0.116
Clavian Dindo Classification	I	5 (41.7%)	1 (7.7%)	3 (12%)	18 (10.6%)	
	II	0	2 (15.4%)	10 (40%)	36 (21.2%)	
	III	0	1 (7.7%)	0	9 (5.3%)	
	IV	0	0	0	3 (1.8%)	
	V	0	0	1 (4%)	2 (1.2%)	
Length of stay in hospital (day/mean ± sd)		13.58±6.8	13.69±7.8	15.88±10.4	13.63±12.2	0.533
Mortality		0	0	1 (4%)	2 (1.2%)	0.641

Group 1, EF < 30%; Group 2, EF 30% to 44%; Group 3, EF 45% to 54%; Group 4, EF > 55%.

an adaptation of the Goldman index, was defined in 1999 [6]. In the study we conducted, the risks were explored using Lee's revised index. Especially in the majority of the patients in Group 1 (58.3%), the Lee's revised index score was found to be 4. There was no significant difference in mortality between Group 1 and the other groups, although there was a significant difference regarding Lee's revised index. This finding can be attributed to the limited number of patients covered by our study.

Surgery-related risk groups have less importance than patient-related factors. Surgical procedures are classified as low (< 1%), moderate (1-5%) and high (> 5%) risk procedures according to the frequency of cardiac events (cardiac death and MI) 30 days after the procedure. According to this classification, major vascular surgical procedures are in the high-risk group [1]. All of our patients were in the moderate risk surgical procedure class according to this classification. No cardiac death or MI was seen when we examined our postoperative patients. Our 3 patients were lost due to surgical complications.

There is a limited number of studies showing the association of LVEF with early postoperative and late postoperative complications in non-cardiac surgical procedures. LVEF is an independent risk factor that determines long-term mortality risks and perioperative results in non-cardiac surgical patients with heart failure and with severely low LVEF (< 30%) [7]. Kantos *et al.* [8] reported in their prospective

Table 4. Univariate logistic regression model analysis with adverse perioperative events as dependent variable

Variable	No comp. (129)	Perioperative events[a] (91)	β	O.R.	95% CI	*P*-value
Age ≥ 65	46 (35.7%)	47 (51.6%)	0.656	1.926	1.116-3.332	0.019*
Sex (M)	77 (59.7%)	61 (67%)	-0.317	0.728	0.16-1.276	0.268
ASA ≥ 3	50 (38.8%)	44 (48.4%)	-0.391	0.676	0.393-1.163	0.157*
Revize lee cardiac index ≥ 3	26 (20.2%)	28 (30.8%)	-0.566	0.568	0.306-1.055	0.073*
Tobacco Use	42 (32.6%)	35 (38.5%)	-0.258	0.772	0.441-1.353	0.366
LVEF ≤ 44	16 (7.3%)	9 (4.1)	0.255	1.290	0.543-3.063	0.564
BMI (kg/m^2) ≥ 25	88 (68.8%)	74 (81.3%)	-0.682	0.505	0.265-0.964	0.038*
FVC < 80	20 (15.5%)	12 (13.2%)	0.189	1.208	0.558-2.614	0.632
FEV1 < 70	10 (7.8%)	10 (11%)	-0.385	0.681	0.271-1.709	0.413
Hypertensıon	38 (29.5%)	25 (27.5%)	0.098	1.102	0.607-2.001	0.748
Diabetes Mellitus	20 (15.5%)	28 (30.8%)	-0.885	2.421	0.215-0.733	0.008*
CABG	8 (6.2%)	9 (9.9%)	-0.507	0.602	0.223-1.626	0.317
CRF	3 (2.3%)	3 (3.3%)	-0.359	0.698	0.138-3.541	0.665
CAD	21 (16.3%)	22 (24.2%)	-0.495	0.610	0.312-1.192	0.148*
COPD	16 (12.4%)	11 (12.1%)	0.029	1.03	0.454-2.337	0.944
History of stoke	3 (2.3%)	3 (3.3%)	-0.359	0.698	0.138-3.541	0.665
Hemotocrit ≤ 30 (%)	11 (9%)	6 (6.7%)	0.327	1.387	0.493-3.903	0.535
Albumin < 3.5 (g/dl)	30 (23.3%)	14 (15.4%)	0.511	1.667	0.827-3.359	0.153*
Creatinin > 1.5 (mg/dl)	11 (8.6%)	7 (7.8%)	-0.109	0.897	0.334-2.411	0.829
Operation Time ≥ 300	39 (30.2%)	46 (50.5%)	-0.858	2.358	0.243-0.740	0.003*
İntraoperative blood transfusion	19 (14.7%)	12 (13.2%)	0.128	1.137	0.522-2.477	0.746

[a]Perioperatif events, peroperatif and postoperatif morbidite and 30 d mortalite; ASA, American Society of Anesthesiologists; LVEF, Leftventricul ejection fraction; BMI, Bady mass index; FVC, Forced expiratory vital capacity; FEV1, Forced Expiratory Volume in the first second; HT, Hypertensıon; DM, Diabetes Mellitus; CABG, Coronary Arter Bypass Greft; CRF, Chronic renal failure; CAD, Coronary artery disease; COPD, chronic obstructive pulmonary disease; CI, Confidence İnterval; *Age ≥ 65, ASA ≥ 3, DM, CAD, Revize lee cardiac index ≥ 3, BMI (kg/m^2) ≥ 25, Albumin < 3.5 (g/dl), and Operation Time ≥ 300 minute were statistically significant on univariate analysis.

Table 5. Multivariate Analysis with adverse perioperative events as dependent variable

Variable	β	*P* value	Odds ratio	95% CI
Age (≥ 65)	-0.851	0.007*	2.341	0.230-0.794
Diabetes Mellitus	-0.899	0.017*	2.457	0.194-0.853
Coronary artery disease	-0.234	0.628	0.791	0.307-2.04
Lee Revised Cardiac Risk index ≥ 3	-0.140	0.752	0.870	0.366-2.064
ASA ≥ 3	0.240	0.550	1.271	0.578-2.795
BMİ ≥ 25 (kg/m^2)	-0.532	0.131	0.587	0.294-1.172
Albumin < 3.5 (g/dl)	0.724	0.076	2.062	0.928-4.583
Operation Time ≥ 300 minute	0.986	0.001*	2.68	0.204-0.682

ASA, American Society of Anesthesiologists; BMI, Body Mass İndex; CI, Confidence İnterval. *Age ≥ 65, DM, and Operation Time ≥ 300 minute were statistically significant on multivariate analysis.

study that patients with an LVEF lower than 29% had a higher surgical mortality risk than those with an LVEF higher than 29%. Moreover, in their prospective study Halm *et al.* [9] found that LVEF lower than 40% was an independent risk factor as was revealed by a revised multivariate analysis of cardiac complications after non-cardiac surgical procedures.

In 2001, Rohde *et al.* [3] found that major cardiac complications were higher in patients with preoperative systolic dysfunction in their study of 570 patients who underwent major non-cardiac surgical procedures. Healy *et al.* [10], in their retrospective study of 174 patients with cardiac failure who underwent moderate and high-risk non-cardiac sur-

gery, concluded that the factors associated with negative perioperative results within the first 30 days following surgery were: older age (> 80 years), diabetes, and severely abnormal LVEF. In our study, we found that LVEF had no effect on perioperative complications in patients with major abdominal tumor surgery. Furthermore, the results of the subgroup analysis we performed revealed that age, DM, and prolonged operation duration were the factors related to perioperative complications.

The limitations of this study include the fact that it was designed as a retrospective study and the limited number of patients with low LVEF.

Conclusion

In our study, we determined the mortality rate as 1.4%. We did not find any relationship between mortality-morbidity, and LVEF. Old age (≥ 65), DM, and prolonged operation time (≥ 300 min) were identified as risk factors associated with morbidity. Mortality was found to be related to surgery-related complications. We believe that major abdominal procedures for GIS malignancies with low LVEF can be performed with acceptable morbidity and mortality rates at experienced centers.

Disclosure of conflict of interest

None.

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