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Title
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Permalink
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Journal
Annals of Surgical Oncology, 27(10)

ISSN
1068-9265

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Publication Date
2020-10-01

DOI
10.1245/s10434-020-08475-w

Peer reviewed

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HHS Public Access
Author manuscript
Ann Surg Oncol. Author manuscript; available in PMC 2021 October 01.

Published in final edited form as:
Ann Surg Oncol. 2020 October ; 27(10): 3772–3780. doi:10.1245/s10434-020-08475-w.

ROBOTIC SURGERY IN THE FRAIL ELDERLY: ANALYSIS OF PERIOPERATIVE OUTCOMES

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Abstract

Purpose: The frail are considered at higher risk for unfavorable surgical outcomes (major complications/mortality). We assessed the safety of and outcomes associated with robotic surgery in the frail elderly undergoing gynecologic procedures.

Methods: We identified patients ≥65 years of age who underwent a robotic procedure from 05/2007-12/2016. Frailty was defined as the presence of at least 3 of 5 frailty factors—more than 5 comorbidities, low physical activity, weight loss, exhaustion, and fatigue. Perioperative outcomes were recorded. We compared variables among frail and non-frail patients and performed a multivariate logistic regression to detect variables associated with major complications (≥ grade 3) or 90-day mortality.

Results: We identified 982 patients—71 frail and 911 non-frail patients. Median age was 71 years. Median BMI was 29.8 kg/m^2. Thirty-four patients (3.5%) had a 30-day readmission. Seventy-seven (7.8%) had a postoperative complication, of which 23 (2.3%) were major. Ninety-day mortality was 0.5%. There were significant differences with regard to age (P<0.001), BMI

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Disclosures: Dr. Leitao is an ad-hoc speaker for Intuitive Surgical. Outside the submitted work, Dr. Chi serves on the medical advisory boards of Apyx Medical Co. and Verthermia Inc; he also had stock investments in Intuitive Surgical and Transenterix (sold in 2018). Outside the submitted work, Dr. Jewell reports other relationships with Summit Biomedical. Outside the submitted work, Dr. Abu-Rustum reports institutional research funding from Stryker and GRAIL.

(P<0.001) and performance status (P<0.001); the frail were more likely to have had surgery for oncologic reasons (P=0.047). There were differences in hospital stay (P<0.001), postoperative (P=0.042) and major complications (P=0.007), and 90-day mortality (P=0.05). At multivariable logistic regression, age ≥85 was associated with major complications. BMI, performance status, and major complications were associated with 90-day mortality.

Conclusion: Frail elderly have longer hospital stays and more complications after surgery than the general population, consistent with the reported literature. Careful selection of surgical candidates is required.

INTRODUCTION

The elderly population is expanding exponentially. In the United States, individuals 65 years of age or older will account for approximately 20% of the population by the year 2030. Over the same time period, the number of individuals older than 75 is expected to triple and the number of individuals older than 85 is expected to double [1]. Seven percent of women older than 65 are considered frail [2], and the higher the level of frailty, the greater the risk of morbidity and mortality [3].

There is no clear consensus on the definition of the term “frailty”. It is used loosely to describe a range of conditions in the elderly, including general debility, cognitive impairment, fatigue, weight loss, muscle loss and weakness, slow walking speed, low levels of physical activity, and progressive decline in body function. Although a definitive definition is lacking, there is some consensus in considering frailty as a health condition with multiple causes and contributors characterized by reduced physiologic function that increases an individual’s vulnerability and likelihood for poor outcomes [3]. The frail elderly are less able to tolerate the stresses of medical illness, hospitalization, and immobility [4]; consequently, they are more likely to experience increased length of hospital stay, complications, and/or mortality [5]. Frailty also adds an extra layer of complexity to surgery; therefore, it is of critical importance to explore ways to accurately recognize frailty and to optimize perioperative care in this patient population.

Recent data have shown the feasibility and safety of the surgical management of elderly patients in several types of cancers, including gynecologic cancers [6,7]. Minimally invasive surgery (MIS) has been shown to be better tolerated than open surgery in select elderly populations [8,9], with improved perioperative outcomes [10-14]. Robotic-assisted surgery, which overcomes many of the limitations of traditional laparoscopy (such as the lack of enhanced 3D visualization or wristed instruments), allows more patients to benefit from MIS [15-19]. However, there are still some concerns with the use of robotic surgery in the elderly population, as data are currently very limited in this area, especially for the frail elderly [20,21]. Many surgeons are cautious about using the robotic platform in this patient population, with apprehensions over longer operative times and hypercapnia due to pneumoperitoneum or the need for prolonged and steep Trendelenburg position, with possible cardiopulmonary consequences [22,23].

Currently, there are no studies in the literature that focus on the role of robotic surgery in the frail elderly population. We previously observed [7] that increased age (≥85 years)

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might be associated with worse clinical outcomes, and we speculated that these unfavorable outcomes could be due to increased frailty caused by multiple comorbidities, impaired physical activity, and reduced performance status. As such, we sought to compare the characteristics of frail elderly versus non-frail elderly patients who underwent gynecologic oncology robotic surgery at Memorial Sloan Kettering Cancer Center (MSK). A secondary objective was to assess if frailty can be considered an unfavorable prognostic factor in robotic surgery.

MATERIALS AND METHODS

After Institutional Review Board approval, we retrospectively identified all patients ≥65 years of age who were scheduled to undergo a planned robotic procedure for a gynecologic indication at MSK from May 2007 to December 2016. Patient and perioperative characteristics were retrospectively extracted from the electronic medical records. All patients, regardless of age, race and type of surgical procedure, were included in our analysis. All surgeries were performed by fellowship-trained attending gynecologic oncology surgeons. Conversion rates were recorded; however, all patients who underwent laparotomy due to conversion were not included in the final analysis.

An institutional surgical secondary event grading system was used to assess complications. Surgery-related complications were defined as those that occurred within 30 days of surgery. Any 30-day readmission was also recorded.

Without a universally accepted definition of frailty, for the purpose of this study, we defined frailty phenotype [24-27] based on the presence of 3 of the following 5 frailty factors: comorbidities (more than 5), low physical activity (cannot walk more than 1 block), weight loss, exhaustion (cannot walk up 1 flight of stairs), and fatigue [3]. These frailty factors are routinely assessed during the nursing and anesthesia perioperative assessment. Weight loss was subjectively reported by patients and/or their family members. We chose to use this definition of frailty due to the retrospective nature of our analysis and because we could capture all 5 factors from the medical records.

The outcomes of the two groups of patients were compared and analyzed with respect to age, body mass index (BMI), Eastern Cooperative Oncology Group (ECOG) performance status, ethnicity, diagnosis, operative details (operating time, uterine size, blood loss), and postoperative outcomes (length of hospitalization, complication rates, readmissions, and mortality). To avoid bias related to the extent of surgery, we also stratified patients according to surgical procedure. A minor procedure was defined as a diagnostic procedure with biopsy or adnexal surgery only. A major procedure was defined as a surgical procedure that included at minimum a hysterectomy and uni-/bilateral salpingo-oophorectomy.

We compared the characteristics of the two groups of patients using chi square or the Fisher exact test, as indicated, for categorical variables and the Mann-Whitney U Test for continuous variables. We also performed a multivariable analysis for factors associated with 90-day mortality and with major perioperative complications, defined as any grade 3 or

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higher complication. Statistical significance was set at $P<0.05$. All statistical analyses were performed using SPSS software.

RESULTS

We identified 1060 patients aged 65 years or older scheduled for robotic surgery with the Gynecology Service, Department of Surgery at MSK. Seventy-eight (7.4%) cases required conversion to laparotomy—58 (5.5%) before and 20 (1.9%) after docking the robotic platform. The most common reason for conversion was presence of adhesions (56.4%), followed by extent of disease (23.1%). No cases were converted due to patient age or frailty-based indications. These cases were not included in the final analysis.

Overall, 982 cases were completed robotically and were included in the final analysis. Patients' clinical characteristics and perioperative details are reported in Table 1. Median age was 71 years (range, 65-96 years). Median BMI was 29.8 kg/m^2 (range, 14.2-65.1 kg/m^2). Most patients were White (84.6%) or Black (5.6%); race was unknown in 6.8% of cases. Most patients had an ECOG performance status score of 0 (74%) or 1 (21%), and 51.6% had undergone prior abdominal surgery. The majority of patients had been treated for endometrial cancer (n=607, 61.8%); 27.2% had undergone surgery for benign indications. A major surgical procedure was performed in most cases (n=851, 86.7%). Median operative time was 159 minutes (range, 40-450 minutes), median blood loss was 50 cc (range, 0-800 cc) and median length of hospital stay was 0 days (range, 0-19 days).

Eighty-one patients (8.2%) experienced one or more perioperative complication, 23 (2.3%) of which were considered major (grade 3 or higher). Four complications (0.4%) occurred intraoperatively. They types and grades of complications are reported in Table 2. Thirty-four patients (3.5%) with a total of 36 complications were readmitted after surgery (Table 3). The most common causes for readmission were gastrointestinal issues (30.6%) and wound-related problems (16.7%).

Five patients (0.5%) died within 90 days of their surgical procedure; 2 were 75 and 77 years old and also deemed frail. In both cases, the cause of death was not specified. An 85-year-old patient died before discharge due to a massive stroke. A 90-year-old patient died from cardiac arrest due to occlusion of the right coronary artery, and a 71-year-old patient died from cancer-related causes.

Seventy-one patients met our study criteria for frailty; 911 patients were considered non-frail. Patient characteristics by frailty status are reported in Table 4. There were no significant differences with regard to race, prior abdominal surgery, type of surgical procedure (minor versus major), estimated blood loss, operative time, intraoperative complications, and readmission rates. The frail compared to non-frail patients were significantly older (median age, 75 vs. 71 years, respectively; $P<0.001$) and heavier (median BMI, 35.1 vs 28.7 kg/m^2, respectively; $P<0.001$). The frail also had significantly worse performance status ($P<0.001$), longer hospital stay ($P<0.001$), were more likely to have undergone surgery for an oncologic diagnosis ($P=0.047$), were more likely to have

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experienced a postoperative (P=0.04) or major complication (P=0.007), and had an increased 90-day mortality risk (P=0.05) (Table 4).

Table 5 summarizes factors associated with the occurrence of major (grade 3-5) perioperative complications. Multivariable analysis showed age ≥85 years was the only factor associated with this unfavorable outcome (adjusted HR, 4.66; 95% CI, 1.44-15.11; P=0.01) after adjusting for other factors such as frailty, having more than 5 comorbidities, BMI, type of procedure (minor versus major procedure), and history of prior abdominal surgery. ECOG performance status was not included in the multivariable analysis, because it demonstrated multi-collinearity with age. We performed a multivariate logistic regression analysis to detect clinical variables that could be prognostic of 90-day mortality (Table 6). Variables significantly associated with 90-day mortality on multivariable analysis included BMI (adjusted HR, 1.16; 95% CI, 1-1.33; P=0.042), ECOG performance status 3-4 (adjusted HR, 7686.53; 95% CI, 10.98-5379219.98; P=0.007), and occurrence of a major complication (adjusted HR, 170.01; 95% CI, 5.94-4866.2; P=0.003).

DISCUSSION

As the population continues to rise and age, gynecologic oncologists increasingly will be tasked with treating older, frailer patients, highlighting the need for better management strategies in this patient population. The available clinical data to guide new treatment strategies, however, are very limited, as these patients are typically underrepresented or excluded from clinical trials [20,21]. Moreover, the data we do have are often inadequate or controversial.

In these patients, the type of surgical approach is important. Surgery may unmask or exacerbate underlying comorbidities, such as renal, cardiac, pulmonary, neurologic or functional issues, leading to unfavorable outcomes. Robotic surgery offers advantages in limiting the impact of predisposing factors in the development of complications, such as with avoiding large fluid shifts or hypothermia with a closed abdomen. Furthermore, the minimally invasive approach has been shown to decrease narcotic and antiemetic use, and to potentially decrease the risk of delirium, postoperative confusion, and disorientation in this high-risk population [28,29].

Many surgeons and anesthesiologists have concern over the potential stress on the body caused by hypercapnia due to pneumoperitoneum or a prolonged Trendelenburg position, which may lead to possible cardiopulmonary consequences or ischemic optic neuropathy [22,23,30]. In our study, there were cases of visual loss or respiratory complications, and only 5 patients experienced cardiovascular complications, none of which occurred intraoperatively. No cases had to be converted or aborted due to cardiovascular or respiratory events.

Robotic surgery appeared to be safe in these frail elderly patients when compared with non-frail patients. Frailty was not related to 90-day mortality on multivariable logistic regression analysis. This was surprising, because in a previous analysis [7] we found that age ≥85 years and BMI were associated with an increased risk of 90-day mortality, which

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we thought might be attributable to an increased prevalence of frailty within this age group. Our current analysis failed to prove this hypothesis, and frailty was not associated with mortality. However, in our multivariable analysis, BMI was associated with 90-day mortality; in particular, it may play a role in decreasing the patient's ability to respond to stressors. As this was a retrospective study, we do not know if this is true, if the small sample size was insufficient to prove a difference, or if other selection biases played a role. Similarly, we found that an ECOG performance status score of ≥3-4 and an occurrence of a major complication were associated with 90-day mortality, but again, we do not know if this result is reliable considering the small sample size. What we can deduce is that frailty goes beyond age. Generally speaking, there are frail 55-year-olds with many comorbidities and poor performance status, and conversely, there are very fit and healthy 85-year-olds with no comorbidities and excellent performance status. This is a good example of why more comprehensive metrics are needed to distinguish between 'frail' and 'non-frail' patients.

In our study, we observed more postoperative (14.1% vs. 7.4%) and major complications (7.0% vs 2.0%) in the frail compared with non-frail patients, respectively. However, our morbidity rates for the frail elderly are still similar, if not better, than those reported for the general elderly population, in which the complication rates from surgery are reported to be as high as 33% [19,22,23,31-36]. Moreover, we did not observe any difference in readmission rates between groups. Operative times and blood loss were similar between the two groups, and similar to those in the reported literature. Our median operative time was 159 minutes, compared with medians ranging from 190-290 minutes in the literature. Median blood loss was 50 cc compared with 50-90 cc in the literature [19,22,23,31-36]. We found that the frail elderly group had longer hospital stays than the non-frail group (1 vs. 0 days, respectively). This finding was consistent with the results of Vaknin et al. [23] who also observed a longer hospital stay (2 versus 1 day, respectively). However, our median hospital length of stay was in the range of 1-3 days reported in the literature for elderly patients [19,22,23,31-36].

Our study results showed a 7.4% conversion to laparotomy rate, mainly due to adhesions or extent of disease. This compares very favorably to data from the Gynecologic Oncology Group (GOG) LAP2 trial, in which the conversion to laparotomy rate for those older than 70 years of age was 28.6% [37], and similar to the rates reported in the Backes [35], Magrina [36], and Vaknin [23] studies. It is important to stress that only 1.9% of cases were converted after docking to the robotic platform, and no cases had to be converted or aborted due to the inability of the patient to tolerate the Trendelenburg position or due to pneumoperitoneum.

The major strength of this study is its specific focus on the role of robotic surgery in the frail elderly population. Limitations include the retrospective nature of the study, which can result in underreporting complications and selection bias. The inclusion of robotic cases during its initial implementation may also have affected the outcomes due to the learning curves of the surgeons.

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CONCLUSION

Robotic-assisted surgery appears to be feasible and safe in the frail elderly patients in our study, as frailty was not associated with 90-day mortality risk on multivariable analysis. However, the frail elderly should be considered high risk, as we observed a longer hospital stay and higher incidence of postoperative and major complications in these patients, even though our rates were comparable to those reported in the literature for minimally invasive surgical approaches in the elderly population. Collaboration between surgical and geriatric societies should be advocated to produce guidelines for adequately selecting surgical candidates and for optimizing the perioperative management of geriatric populations in a multidisciplinary setting.

ACKNOWLEDGEMENTS

Funding: The study was funded in part by the National Institutes of Health/National Cancer Institute Memorial Sloan Kettering Cancer Center Support Grant (P30 CA008748).

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SYNOPSIS

Robotic-assisted surgery appears to be feasible and safe in the frail elderly population. However, these patients should be considered high risk and carefully selected for surgery.

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Table 1:

Characteristics of robotically completed cases (N=982)

Variable	n	%
Median age, years (range)	71	65-96
Race		
American Indian/Alaska Native	1	0.1
White	831	84.6
Asian	28	2.9
Black	55	5.6
Unknown	67	6.8
Median body mass index, kg/m^2 (range)	29.8	14.2-65.1
ECOG performance status		
0	727	74.0
1	206	21.0
2	41	4.2
3	7	0.7
4	1	0.1
5	0	0.0
Previous abdominal surgery	507	51.6
Indication for surgery		
Benign	64	6.5
Uterine hyperplasia	41	4.2
Uterine cancer	607	61.8
Breast cancer/risk-reducing surgery	9	0.9
Benign adnexal mass	147	15.0
Ovarian/fallopian tube cancer	74	7.5
Cervical dysplasia	6	0.6
Cervical cancer	22	2.2
Two gynecologic primaries	4	0.4
Lymphoma	4	0.4
Other	4	0.4
Procedure		
Minor	131	13.3
Major	851	86.7
Median estimated blood loss, cc (range)	50	0-800
Median uterine size, g (range) [#]		
Median (range)	91	27-740
Median operating room time, min (range)	159	40-450
Median length of hospital stay, days (range)	0	0-19
Readmission within 30 days	34	3.5
Death within 90 days	5	0.5

ECOG, Eastern Cooperative Oncology Group

[#]only 839 patients were evaluated for uterine size

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Table 2:

Complications (n=83) in overall cohort[#]

Intraoperative (n=4)						Total N (%)
	Grade 1	**Grade 2**	**Grade 3**	**Grade 4**	**Grade 5**	
Genitourinary	0	0	3	0	0	3 (75%)
Hematologic/vascular	0	0	1	0	0	1 (25%)
Postoperative (n=79)						
	Grade 1	**Grade 2**	**Grade 3**	**Grade 4**	**Grade 5**	
Cardiovascular	1	2	1	0	1	5 (6.3%)
Gastrointestinal	3	5	6	0	0	14 (17.7%)
Genitourinary	18	1	0	0	0	19 (24%)
Hematologic/vascular	2	5	3	0	0	10 (12.7%)
Neurologic	1	1	1	0	1	4 (5.1%)
Intra-abdominal collection	0	2	4	0	0	6 (7.6%)
Pulmonary	1	0	0	0	0	1 (1.3%)
Wound/skin	18	0	2	0	0	20 (25.3%)

[#]83 complications occurred among 81 patients

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Table 3:

Reasons for readmission (n=34 patients)[#]

Reason for readmission (n=36)	n	(%)
Gastrointestinal issues	11	30.6
Wound/skin issues	6	16.7
DVT/PE	2	5.6
Pneumonia	1	2.8
Urologic issues	4	11.1
Bleeding/hematoma	5	13.9
Intra-abdominal collections	4	11.1
Neurologic issues	2	5.6
Other	1	2.8

DVT, deep vein thrombosis; PE, pulmonary embolism

[#]some patients had more than one reason for readmission

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Table 4:

Comparison of frail versus non-frail patients

Variable	NON-FRAIL n=911		FRAIL n=71		*P*
Median age, years (range)	71	65-96	75	66-92	<0.001
Race					
American Indian/Alaska Native	1	0.1	0	0.0	0.298
White	771	84.6	60	84.5	
Asian	28	3.1	0	0.0	
Black	48	5.3	7	9.9	
Unknown	63	6.9	4	5.6	
Median BMI, kg/m^2 (range)	28.7	14.2-65.1	35.1	20-56.6	<0.001
ECOG performance status					
0	720	79.1	6	8.5	<0.001
1	176	19.3	30	42.3	
2	13	1.4	28	39.4	
3	1	0.1	6	8.5	
4	0	0.0	1	1.4	
5	0	0.0	0	0.0	
Previous abdominal surgery	472	51.8	35	49.3	0.683
Indication for surgery					
Benign	62	6.8	2	2.8	0.047
Uterine hyperplasia	41	4.5	0	0.0	
Uterine cancer	554	60.8	53	74.6	
Breast cancer/risk-reducing	9	1.0	0	0.0	
Benign adnexal mass	143	15.7	4	5.6	
Ovarian/fallopian tube cancer	66	7.2	8	11.3	
Cervical dysplasia	5	0.5	1	1.4	
Cervical cancer	21	2.3	1	1.4	
Two gynecologic primaries	4	0.4	0	0.0	
Lymphoma	3	0.3	1	1.4	
Other	3	0.3	1	1.4	
Procedure					
Minor	124	13.6	7	9.9	0.370
Major	787	86.4	64	90.1	
Median estimated blood loss, cc (range)	50	0-800	50	10-300	0.070
Median uterine size, g (range) [#]	n=777 90	27-740	n=62 115	39-429	0.015
Median operating room time, min (range)	154	40-476	149	61-417	0.700
Median length of hospital stay, days (range)	0	0-19	1	0-11	<0.001
Intraoperative complication	4	0.4	0	0	0.576
Postoperative complication	67	7.4	10	14.1	0.042

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Variable	NON-FRAIL n=911		FRAIL n=71		*P*
Major complication (grade 3-5)	18	2.0	5	7	0.007
Readmission within 30 days	30	3.3	4	5.6	0.299
Death within 90 days	3	0.3	2	2.8	0.05

ECOG, Eastern Cooperative Oncology Group

[#]only 839 patients were evaluated for uterine size

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Table 5.

Multivariable analysis of factors associated with major (grade 3-5) perioperative complications

Variable	Univariate		Multivariable	
	HR (95% CI)	***P***	**Adjusted HR (95% CI)**	***P***
Age group				
65-74	Reference	--	Reference	--
75-84	2.76 (0.17-44.26)	0.474	1.18 (0.43-3.27)	0.747
85+	29.74 (2.65-334.09)	0.006	4.66 (1.44-15.11)	0.01
BMI (kg/m^2) - continuous	0.98 (0.92-1.04)	0.570	0.97 (0.91-1.04)	0.420
ECOG performance status				
0	Reference	--		
1	1.42 (0.54-3.71)	0.472		
2	1.18 (0.15-9.19)	0.871		
3	7.9 (0.89-69.74)	0.063		
4	0 (0-0)	1.000		
5	0 (0-0)	1.000		
5 or more comorbidities				
No	Reference		Reference	--
Yes	0.57 (0.61-4.04)	0.349	1 (0.3-3.31)	0.996
Prior abdominal surgery				
No	Reference	--	Reference	--
Yes	1.22 (0.53-2.82)	0.635	1.39 (0.59-3.25)	0.443
Procedure				
Major	Reference	--	Reference	--
Minor	3.45 (0.46-25.81)	0.228	3.52 (0.46-26.9)	0.225
Frail				
No	Reference	--	Reference	--
Yes	3.76 (1.35-10.44)	0.011	3.25 (0.88-12.02)	0.077

BMI, body mass index; ECOG, Eastern Cooperative Oncology Group

All variables were tested for multicollinearity. Clinically significant variables and variables with p<0.2 on univariate analysis were included in the multivariable analysis.

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Table 6.

Multivariable analysis of factors associated with 90-day mortality

Variable	Univariate		Multivariable	
	HR (95% CI)	*P*	Adjusted HR (95% CI)	*P*
Age group				
65-74	Reference	--	Reference	--
75-84	5.47 (0.49-60.59)	0.166	0.43 (0.004-47.99)	0.729
85+	29.44 (2.62-330.25)	0.006	20.39 (0.86-484.28)	0.062
BMI (kg/m^2) - continuous	1.11 (1.02-1.21)	0.019	1.16 (1.005-1.33)	0.042
ECOG performance status				
0	Reference	--	Reference	--
1-2	5.79 (0.52-64.13)	0.152	4.66 (0.16-133.25)	0.369
3-4	259.67 (20.66-3263.89)	<0.001	7686.5 (10.98-5379219.9)	0.007
5 or more comorbidities				
No	Reference	--	Reference	--
Yes	6.53 (1.08-39.36)	0.041	1.926 (0.08-44.86)	0.683
Procedure				
Major	Reference	--		
Minor	0.58 (0.06-5.25)	0.629		
Major complication (grade 3-5)				
No	Reference	--	Reference	--
Yes	55.02 (8.84-342.34)	<0.001	170.01 (5.94-4866.26)	0.003
Frail				
No	Reference	--	Reference	--
Yes	8.47 (1.39-51.44)	0.020	0.03 (0-3.83)	0.152

BMI, body mass index; ECOG, Eastern Cooperative Oncology Group

All variables were tested for multicollinearity. Clinically significant variables and variables with p<0.2 on univariate analysis were included in the multivariable analysis.