

Use of a Comprehensive Geriatric Assessment to Predict Short-Term Postoperative Outcome in Elderly Patients With Colorectal Cancer

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Purpose: This study was conducted to identify the effectiveness of a preoperative comprehensive geriatric assessment (CGA) for predicting postoperative morbidity in elderly patients who underwent surgery for colorectal cancer.

Methods: Elderly patients (≥ 70 years old) who underwent surgery for colorectal cancer at a tertiary hospital in Korea were identified, and their cases were analyzed using data from a prospectively collected database to establish an association between major postsurgical complications and 'high-risk' patient as defined by the CGA.

Results: A total of 240 patients, with a mean age of 76.7 ± 5.2 years, were enrolled. Ninety-five patients (39.6%) were classified as "high-risk" and 99 patients (41.3%) as having postoperative complications. The univariate analysis indicated that risk factors for postoperative complications were age, American Society of Anesthesiologists physical status classification, serum hemoglobin, carcinoembryonic antigen, cancer stage, and "high-risk" status. The multivariable analyses indicated that "high-risk" status (odds ratio, 2.107; 95% confidence interval, 1.168–3.804; $P = 0.013$) and elevated preoperative carcinoembryonic antigen (odds ratio, 2.561; 95% confidence interval, 1.346–4.871, $P = 0.004$) were independently associated with postoperative complications. A multivariable analysis of the individual CGA domains indicated that high comorbidities and low activities of daily living were significantly related with postoperative complications.

Conclusion: A preoperative CGA indicating "high-risk" was associated with major postoperative complications in elderly patients who underwent surgery for colorectal cancer. Thus, using the CGA to identify elderly colorectal-cancer patients who should be given more care during postoperative management may be clinically beneficial.

Keywords: *Colorectal neoplasms; Comprehensive geriatric assessment; Complication*

INTRODUCTION

Korea and many other developed countries have increasing percentages of elderly people. The Korea National Statistical Office

has predicted that the elderly will account for 38.2% of the Korean population in 2050, even higher than the 37.7% expected in Japan [1]. As the aging population increases, the surgery rate for elderly patients is also increasing, which is made possible by improvements in anesthetic and surgical techniques. In the United States, more than half of all operations are performed on elderly patients (>65 years old), and this proportion is increasing [2]. In Korea, the number of individuals older than 60 years of age who were eligible for surgery has increased from 0.47 million in 2004 to 1.05 million in 2014 [1].

Furthermore, elderly patients who underwent head and neck, thoracic, and hip fracture surgery had higher rates of postoperative complications than the general population [3-5]. This may be explained by the greater frailty of the elderly, who often have de-

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creased physiological reserves in multiple organ systems and numerous comorbid conditions. Frail elderly patients are more likely to suffer from postoperative complications such as cardiac problems, pneumonia, and deep vein thrombosis. In spite of the high rate of postoperative complications in the elderly, no optimal tool that accurately predicts postoperative morbidity is available to assess preoperative risks and physiological reserves of the elderly.

Geriatricians initially designed the comprehensive geriatric assessment (CGA) as a multidimensional tool to examine the general health status of the elderly based on validated geriatric scales and tests that examine diverse health problems. The results of the CGA can allow development of individualized geriatric intervention programs, and in many sub-fields of geriatrics, the CGA is used to evaluate geriatric conditions that are associated with frailty [6]. The CGAs used in previous studies assessed the functional, physiological, mental, and socioeconomic features of elderly patients [6-8]. However, the efficacy of the CGA as a preoperative assessment tool has not been validated for surgery patients. Some previous studies used the CGA to study patients with heterogeneous conditions, including those who underwent orthopedic, neurological, cardiac, or abdominal surgery [7, 8].

Colorectal cancer (CRC) is a major cause of cancer-related deaths in Korea, and its incidence has been increasing over the past 25 years [9]. The incidence of CRC reached a peak in the 1970s, and CRC is now the most common malignancy in elderly females and the third-most common malignancy in males. Thus, the number of elderly patients undergoing surgery for CRC has seen a steep increase [9]. However, the usefulness of the CGA in predicting the outcome in elderly patients with CRC has not yet been evaluated. Thus, the purpose of the present study was to identify the efficacy of a preoperative CGA for predicting postoperative morbidity in elderly patients who underwent surgery for CRC.

METHODS

Patient selection

A retrospective review of a prospective, Institutional Review Board-approved database was performed to identify elderly patients (≥ 70 years old) who had undergone major elective surgery for primary CRC in the Seoul National University Bundang Hospital from 1 March 2009 to 28 February 2014. All patients who had undergone elective CRC surgery and had preoperative CGA results were enrolled. Patients were excluded if they had taken a CGA survey after surgery or more than 6 months prior to surgery, if they had undergone emergency surgery, or if their CGA results were incomplete. The baseline characteristics of patients included epidemiologic data, medical history, and perioperative and laboratory characteristics such as white blood cell count, hemoglobin, platelet count, prothrombin time, albumin, glucose, aspartate transaminase and alanine transaminase, creatinine, and pre/postoperative carcinoembryonic antigen (CEA).

CGA protocol

A preoperative CGA was used to assess the condition of each patient's health within 6 months of surgery. All patients were interviewed face-to-face by the geriatric team, which consisted of geriatricians, nurse specialists, dietitians, and pharmacists. The preoperative CGA had 8 domains: burden of comorbidity (Charlson Comorbidity Index, CCI), poly-pharmacy, physical function according to activities of daily living (ADL), instrumental ADL (IADL), cognitive status (Mini-Mental State Examination), risk of postoperative delirium (Nursing Delirium Screening Scale), Korean Geriatric Depression Scale, and nutritional status (mini nutritional assessment). The definition of "deficit" in each domain was the same as in our previous studies [7, 8]: a score of 3 or more for comorbidities [10], the regular use of 8 or more drugs [11], poor physical function assessed by using the ADL, poor physical function assessed by using the IADL [12], cognitive dysfunction assessed by using the Korean version of the Mini-Mental State Examination, severe depression, and malnutrition.

We defined a "high-risk" patient as one who had deficits in two or more domains. A surgical complication with Clavien-Dindo grade II or higher within 30 days of surgery was classified as a major complication [13], and a grade I complication as uneventful.

Ethical approval

The Institutional Review Board of Seoul National University Bundang Hospital approved this study prior to commencement of data collection and analysis (approval number: B-1504-294-103) and waived the informed consent requirement because it was a retrospective review.

Statistical analysis

The associations between CGA domains, "high-risk" status, demographic data, laboratory findings, and postoperative major complications were analyzed by using chi-square tests. The associations between explanatory variables and postoperative major complications were determined by using multiple logistic regression analyses with backward elimination. Univariate and multivariate analyses were also used to assess the relationships between each CGA domain and postoperative major complications. A *P*-value less than 0.05 was considered statistically significant. All statistical analyses were performed using IBM SPSS ver. 18.0 (IBM Co., Armonk, NY, USA).

RESULTS

Patient characteristics

A total of 324 elderly patients underwent surgery for CRC during the study period. Eighty-four patients were excluded because they received emergency operations ($n = 4$) or did not receive a preoperative CGA ($n = 80$), so 240 patients were ultimately enrolled (Table 1). The mean age was 76.7 years (range, 70–96 years), and 6 patients were older than 90 years of age. Sixty percent of the pa-

Table 1. Baseline demographic, clinical, and laboratory characteristics of elderly patients who underwent surgery for colorectal cancer (n = 240)

Characteristic	Value
Sex	
Male	138 (57.5)
Female	102 (42.5)
Age (yr)	
70–79	180 (75.0)
80–89	54 (22.5)
≥90	6 (2.5)
Mean ± SD	76.7 ± 5.20
Body mass index (kg/m ²)	
≤25	161 (67.0)
>25	79 (33.0)
Mean ± SD	23.8 ± 3.67
Hypertension	
No	98 (40.8)
Yes	142 (59.2)
Diabetes	
No	190 (79.2)
Yes	50 (20.8)
ASA physical status classification	
I	39 (16.3)
II	174 (72.5)
≥III	27 (11.2)
Prior operation	
No	99 (41.2)
Yes	141 (58.8)
Tumor location	
Colon	150 (62.5)
Rectum	90 (37.5)
Pathologic stage	
0–1	53 (22.1)
2	52 (21.7)
3	110 (45.8)
4	25 (10.4)
Surgical approach	
Open	80 (33.3)
Laparoscopic	160 (66.7)
Co-operation	
No	186 (77.5)
Yes	54 (22.5)

(Continued to the next)

Table 1. Continued

Characteristic	Value
White blood cell (×10 ³ /mm ³)	
≤4	212 (8.3)
>4	28 (11.7)
Hemoglobin (g/dL)	
≥12.0	122 (50.8)
<12.0	118 (49.2)
Platelets (/ μ L)	
≥130,000	224 (93.3)
<130,000	16 (6.7)
PT INR	
≤1.2	231 (96.3)
>1.2	9 (3.7)
Serum Albumin (g/dL)	
≥3.3	229 (95.4)
<3.3	11 (4.6)
Glucose (mg/dL)	
≤110	147 (61.3)
>110	90 (38.7)
AST (U/L)	
≤40	227 (94.6)
>40	13 (5.4)
ALT (U/L)	
≤40	232 (96.7)
>40	8 (3.3)
Serum creatinine (mg/dL)	
≤1.2	174 (72.5)
>1.2	66 (27.5)
Preoperative CEA (ng/mL)	
≤5	159 (66.3)
>5	60 (33.7)
Postoperative CEA (ng/mL)	
≤5	207 (86.3)
>5	24 (13.7)

Values are presented as number (%) unless otherwise indicated. SD, standard deviation; ASA, American Society of Anesthesiologists; PT, prothrombin time; INR, international normalized ratio; AST, aspartate aminotransferase; ALT, alanine aminotransferase; CEA, carcinoembryonic antigen.

tients had hypertension, and 20% had diabetes mellitus; moreover, most patients had American Society of Anesthesiologists (ASA) physical status classification of I (healthy) or II (mild systemic disease). Two-thirds of the patients had tumors in the colon, and most patients underwent laparoscopic surgery (66.7%). Laboratory findings indicated that about half of the patients had

preoperative anemia; 10 of those patients were given transfusions before surgery. The serum albumin level, reported by several studies as an independent predictor for morbidity [14-16], was normal in most patients. About one-quarter of the patients had elevated levels of serum creatinine, but only one had chronic renal insufficiency and needed dialysis. One-third of the patients had elevated levels of preoperative CEA.

CGA results

Overall, 95 of the enrolled 240 patients (39.6%) had deficits in 2 or more domains on the preoperative CGA and were categorized as “high-risk” patients (Table 2). Analysis of the individual domains indicated that nearly half of the patients had a score of 3 or more for comorbidities (diabetes mellitus, cerebrovascular disease, chronic pulmonary disease, etc.), about 10% were dependent in terms of physical activity measured by using the ADL or the IADL, 42.5% had mild or severe decreases in cognitive function, and a small number had depression (9.2%) and delirium (3.8%).

Postoperative complications

Of the 240 enrolled patients, 183 patients (76.3%) experienced postoperative morbidities, and 99 (41.3%) had major complications (grades II–V) that required medical or surgical intervention (Table 3). Two patients (0.8%) died, one from postoperative pneumonia and the other from multiorgan failure following abdominal sepsis. The most common complication was mild electrolyte imbalance, but that spontaneously resolved in all patients without specific treatment. Among the major complications, voiding difficulty (10%) was the most common. This complication was resolved by using urinary catheter reinsertion for more than 3 days to rest the bladder (17 patients) and administration of an α 1-adrenergic receptor antagonist (24 patients).

Univariate and multivariate analysis of factors associated with major postoperative complications

Univariate analyses indicated that advanced age, higher ASA physical status classification, more advanced CRC stage, presence of anemia, elevated serum CEA level, and “high-risk” based on the CGA were significantly associated with major complications (Table 4). These 6 significant variables were analyzed by using multiple logistic regression analyses with backward elimination, in which the factor that had the smallest correlation to postoperative major complications was removed in each stage (Table 5). The results indicated that “high-risk” based on the CGA (odds ratio [OR], 2.107; 95% confidence interval [CI], 1.168–3.804; $P = 0.013$) and a preoperative CEA level of more than 5 ng/mL (OR, 2.561; 95% CI, 1.346–4.871; $P = 0.004$) were significantly and independently associated with postoperative complications.

We also performed univariate and multivariate analyses to evaluate the effect of each deficient domain on the CGA for grades II–V complications (Table 6). The results indicate that a score of 3 or more for comorbidities (OR, 2.237; 95% CI, 1.183–4.230; $P =$

Table 2. CGA^a in eight domains and identification of “high-risk” patients^b

Variable	Value
Comorbidities	
0–2	132 (55.0)
≥3	108 (45.0)
Mean ± SD	2.76 ± 1.14
Medication	
0–7	207 (86.3)
≥8	33 (13.8)
Mean ± SD	4.04 ± 3.59
ADL	
Dependent	18 (7.5)
Independent	222 (92.5)
IADL	
Dependent	26 (10.8)
Independent	214 (89.2)
MMSE	
0–24	102 (42.5)
≥25	132 (57.5)
Mean ± SD	23.5 ± 5.01
SGDS	
0–9	210 (87.5)
≥10	22 (9.2)
Mean ± SD	3.65 ± 3.50
Delirium	
0–1	205 (85.4)
≥2	9 (3.8)
Mean ± SD	0.24 ± 0.56
MNA	
<17	15 (6.3)
17–24	83 (34.6)
>24	141 (58.6)
Mean ± SD	23.8 ± 4.38
High risk	
No	145 (60.4)
Yes	95 (39.6)

Values are presented as mean ± standard deviation (range) or number (%).

CGA, comprehensive geriatric assessment; ADL, physical function according to activities of daily living; IADL, instrumental ADL; MMSE, Mini-Mental State Examination; SGDS, Korean Geriatric Depression Scale; MNA, mini nutritional assessment; SD, standard deviation.

^aCGA indicates the “deficit” group in each domain. ^bHigh-risk patients are those that had deficits in two or more domains.

0.013) and a high ADL score (OR, 16.369; 95% CI, 1.233–217.2; $P = 0.034$) were significantly and independently associated with a

Table 3. Grades of postoperative complications^a in elderly patients who underwent surgery for colorectal cancer

Complication	Grade					Total
	I	II	III	IV	V	
Electrolyte imbalance	36	–	–	–	–	36
Self-voiding difficulty	–	24	–	–	–	24
Unknown fever	15	4	–	–	–	19
Wound problem	8	–	6	–	–	14
Ileus	3	7	1	1	–	12
Atelectasis	10	1	–	–	–	11
Transfusion	–	9	–	–	–	9
Pneumonia	–	5	–	2	1	8
Cardiac problem	–	5	1	2	–	8
Nausea & vomiting	7	–	–	–	–	7
Delirium	–	7	–	–	–	7
Bleeding	2	3	–	–	–	5
DVT & PTE	1	3	–	–	–	4
Fluid collection	–	–	4	–	–	4
Anastomotic leakage	–	–	–	2	1	3
UTI	–	3	–	–	–	3
URI	1	2	–	–	–	3
Acute cholecystitis	–	–	–	1	–	1
Others	1	3	1	–	–	5
Total, n (%)	84 (35.0)	76 (31.7)	13 (5.4)	8 (3.3)	2 (0.8)	183 (76.3)

Gr, grade; DVT, deep vein thrombosis; PTE, pulmonary thromboembolism; UTI, urinary tract infection; URI, upper respiratory infection.

^aClavien-Dindo classification of surgical complications [13].

risk of major complications.

DISCUSSION

The main finding of the present study is that the results of a preoperative CGA can predict postoperative complications in elderly patients who undergo surgery for CRC. Additionally, among the eight domains in the CGA, the comorbidities and the ADL domains were significantly and independently associated with major postoperative complications. Previous studies reported that advanced age, advanced tumor stage, emergency surgery, blood transfusion, malnutrition, diabetes, and pre-existing cardiac pathology were risk factors for postoperative complications in elderly patients with CRC [17-19].

Traditional health scoring systems are widely used to evaluate elderly patients before major abdominal surgery. These systems include the ASA physical status classification, the acute physiology and chronic health evaluation (APACHE II), estimates of physiologic ability and surgical stress, and the physiological and operative severity score for the enumeration of mortality and morbidity. As the CGA has been adopted in various medical fields, some studies have reported on the use of the CGA as a pre-

operative assessment [7, 8]. As far as we know, the present study is the largest study of patients who underwent elective surgery for CRC and were given preoperative CGAs.

Our results indicate that an elevated preoperative level of serum CEA was significantly associated with postoperative complications. However, in no previous studies was any relationship between preoperative CEA and postoperative complications in elderly patients reported or explained. Because tumor burden may have an indirect effect on morbidity, patients with large tumors usually have elevated CEA levels; furthermore, difficulty during surgery due to the large tumor size may lead to more frequent postoperative complications [20]. Thus, elevated CEA level may be associated with more frequent postoperative complications.

Our results indicated that advanced age and ASA physical status classification were not associated with postoperative complications. Previous studies reported that biological age was a more significant prognostic factor than chronological age in elderly patients [21, 22]. We found that 5 of the 6 patients who were at least 90 years of age recovered without severe postoperative complications; one 90-year-old male, classified as “high risk” based on the CGA results, had pneumonia and died in spite of aggressive medical treatment and intensive care unit care. This finding supports

Table 4. Univariate analysis of factors associated with major postoperative complications in elderly patients who underwent surgery for colorectal cancer

Variable	No.	Uneventful recovery (grade 0–I) (n = 141)	Major complication (grade II–V) (n = 99)	P-value
Sex				1.000
Male	138	81 (57.4)	57 (57.6)	
Female	102	60 (42.6)	42 (42.4)	
Age (yr)				0.006
70–79	180	115 (81.6)	65 (65.7)	
80–89	54	25 (17.7)	29 (29.3)	
≥90	6	1 (0.7)	5 (5.1)	
Body mass index (kg/m ²)				1.000
≤25	161	95 (67.4)	66 (66.7)	
>25	79	46 (32.6)	33 (33.3)	
Hypertension				1.000
No	98	58 (41.1)	40 (40.4)	
Yes	142	83 (58.9)	59 (59.6)	
Diabetes				0.520
No	190	114 (80.9)	76 (76.8)	
Yes	50	27 (19.1)	23 (23.2)	
ASA physical status classification				0.005
I	39	25 (17.7)	14 (14.1)	
II	174	108 (76.6)	66 (66.7)	
≥III	27	8 (5.7)	19 (19.2)	
Tumor location				0.590
Colon	150	86 (61.0)	64 (64.6)	
Rectum	90	55 (39.0)	35 (35.4)	
Pathologic stage				0.006
0–1	53	39 (27.7)	14 (14.1)	
2	52	32 (22.7)	20 (20.2)	
3	110	62 (44.0)	48 (48.5)	
4	25	8 (5.7)	17 (17.2)	
Hemoglobin (g/dL)				0.004
≥12.0	122	83 (58.9)	39 (39.4)	
<12.0	118	58 (41.1)	60 (60.6)	
Preoperative CEA (ng/mL)				<0.001
≤5	159	105 (82.0)	54 (59.3)	
>5	60	23 (18.0)	37 (40.7)	
High-risk				0.001
No	145	98 (69.5)	47 (47.5)	
Yes	95	43 (30.5)	52 (52.5)	

Values are presented as number (%).

ASA, American Society of Anesthesiologists; CEA, carcinoembryonic antigen.

Table 5. Multivariate analysis of factors associated with major postoperative complications in elderly patients who underwent surgery for colorectal cancer

Characteristic	OR	95% CI	P-value
No. of deficient domains in CGA			0.013
0-1 (low risk)	1	Reference	
≥2 (high risk)	2.107	1.168-3.804	
Preoperative CEA (ng/mL)			0.004
≤5	1	Reference	
>5	2.561	1.346-4.871	

OR, odds ratio; CI, confidence interval; CEA, carcinoembryonic antigen.

the selection of “high risk” patients based on CGA rather than chronological age when planning surgery for elderly patients. The ASA physical status classification is also useful in evaluating elderly surgery patients [23, 24]. Some recent studies suggested there should be another method rather than ASA physical status classification [21, 25, 26]. The ASA physical status classification was not predictive of morbidity in the present study. The reasons may be the facts that approximately 90% of our patients were classified as ASA physical status classification I (healthy) or II (mild systemic disease) and the ASA physical status classification may not have the sensitivity to detect differences between those 2 groups.

Table 6. Univariate and multivariate analyses of the relationship of deficit in each CGA domain and occurrence of major postoperative complications

Characteristic	No.	Uneventful recovery (grade 0-I) (n = 141)	Major complication (grade II-V) (n = 99)	P-value	OR	95% CI	P-value
Co-morbidity				0.004			0.013
0-2	127	86 (61.0)	41 (41.4)		1	Reference	
≥3	113	55 (39.0)	58 (58.6)		2.237	1.183-4.230	
Medications				0.056			0.962
0-7	207	127 (90.1)	80 (80.8)		1	Reference	
≥8	33	14 (9.9)	19 (19.2)		1.023	0.392-2.673	
ADL				<0.001			0.034
Dependent	28	6 (4.3)	22 (22.2)		16.369	1.233-217.2	
Independent	212	135 (95.7)	77 (77.8)		1	Reference	
IADL				0.01			0.807
Dependent	26	9 (6.4)	17 (17.2)		0.721	0.052-9.915	
Independent	214	132 (93.6)	82 (82.8)		1	Reference	
MMSE				0.18			0.945
0-24	102	56 (40.0)	46 (48.9)		0.977	0.509-1.876	
≥25	132	84 (60.0)	48 (51.1)		1	Reference	
SGDS				0.36			0.620
0-9	210	129 (92.1)	81 (88.0)		1	Reference	
≥10	22	11 (7.9)	11 (12.0)		1.302	0.459-3.695	
Delirium				<0.001			-
0-1	205	129 (100)	76 (89.4)		1	Reference	
≥2	9	0 (0.0)	9 (10.6)		-	-	
MNA				0.08			0.183
<17	15	7 (5.0)	8 (8.1)		0.105	0.007-1.642	
17-24	83	42 (30.0)	41 (41.4)		1.281	0.657-2.500	
>24	141	91 (65.0)	50 (50.5)		1	Reference	

Values are presented as number (%).

CGA, comprehensive geriatric assessment; OR, odds ratio; CI, confidence interval; ADL, physical function according to activities of daily living; IADL, instrumental ADL; MMSE, Mini-Mental State Examination; SGDS, Korean Geriatric Depression Scale; MNA, mini nutritional assessment.

This study only examined patients who had elective surgery. In emergency operations, elderly patients have a much greater chance of suffering from postoperative complications than younger patients. In particular, elderly patients who underwent emergency operations were reported to have 3 to 10 times higher morbidity and mortality than those who were well-prepared and underwent elective operations [27]. No studies have yet assessed the predictive value of the CGA for postoperative outcome in elderly patients in emergency settings. However, such a study would be difficult because of the lack of sufficient time to evaluate patients' conditions by interview.

One novel finding in the present study is that the eight domains of the CGA have different clinical significance. Greater independence in daily living (high ADL score) and fewer comorbidities were predictive of an uneventful recovery after surgery for CRC. Interestingly, all patients at high risk of developing delirium had major postoperative complications, although this domain showed no statistical significance on the multivariate analysis. Some previous studies did report that preoperative cognitive dysfunction was related with postoperative complications in elderly patient [28, 29].

The present study had several limitations. First, 80 patients did not receive preoperative CGA during the study period. The reasons for this included patient refusal, absence of a physician responsible for the CGA, and patient unavailability during the preoperative workup at the outpatient clinic. Second, this study also had bias because it was a retrospective, single-center study. However, we performed backward substitution methods with multivariate logistic regression without over fitting to reduce statistical bias.

In conclusion, the results of a preoperative CGA were predictive of major postoperative complications in elderly patients undergoing surgery for CRC. Thus, its use may be clinically beneficial for detecting "high-risk" patients so that they can be provided with more careful postoperative management following surgery.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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