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Review Article

Effectiveness of Geriatric Assessment in Predicting Postoperative Morbidity after Laparoscopic Surgery in Older Patients: A Systematic Review

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SUMMARY

The main aim was to review the results of studies investigating individual domains of geriatric assessment (GA), and GA as a whole, among older patients undergoing laparoscopic surgery. A systematic literature search was performed for papers published between 2009 and 2020. Ten studies were evaluated, including 1940 patients. The activities of daily living (ADL) or the instrumental activities of daily living (I-ADL), was used in 90% of studies, followed by the geriatric depression score (GDS) (80%), the Mini-Mental State Examination (MMSE) (70%), polypharmacy (70%), the Mini Nutritional Assessment (MNA) (60%), the Charlson Comorbidity Index (CCI) (50%), the cumulative illness rating scale (CIRS) (20%), the Blessed Orientation-Memory-Concentration (BOMC) score (10%) and the Clock Drawing Test (CDT) (10%). Only dependency in the functional domain could be recognized as a reliable risk factor for postoperative complications in the majority of the studies. All authors have confirmed the effectiveness of a cumulative GA (odds ratio 3.1–6.0). Cumulative GA is recommended to predict the morbidity of the older patient after laparoscopic surgery. For the individual domains (apart from physical function) the results are too inconsistent to reach any clinical conclusion.

1. Introduction

Laparoscopy is considered a milestone in the development of surgery. However, there is still lack of good quality data on its use in older patients, particularly in the frail population. Schiphorst et al., analyzing representation of the elderly in trials of laparoscopic surgery for colorectal cancer, showed that 44% studies excluded the elderly and in 86% of the trials the average age of participants was < 70 years.[1]

At present, older patients account for half of all adult operations, but about 80% of postoperative complications.[2,3] The chronological age alone and the routine format of present preoperative evaluation often do not provide adequate information needed for optimal and tailored treatment. To help guide treatment decisions a geriatric assessment (GA) was introduced. The GA assesses individual domains (physical function, nutrition, comorbidities, psychosocial aspects, cognitive function, polypharmacy) of major impact on older people's capabilities.[4] It facilitates initial assessment of the older patient's condition, identification of previously unknown health problems, diagnosis of frailty, and assessment of the likelihood of postoperative complications.[5] However, it is not established which of the GA components are most useful for predicting postoperative complications in patients undergoing laparoscopic surgery.

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2. Aim

The main aim of this review is to summarize results of studies investigating individual domains of GAs and the GA as a whole among older patients undergoing laparoscopic surgery.

3. Material and methods

Two authors searched idependently electronic databases (PubMed, Cochrane, Ovid, NICE, CBM, CINAHL Complete) to find relevant studies. The search criteria includes articles published between January 2009 and March 2020 and with keyword subject terms: ("geriatric assessment" OR "comprehensive geriatric assessment" OR "GA" OR "CGA") AND ("gastrointestinal" OR "abdominal" OR "colorectal") AND ("surgery" OR "operation" OR "laparoscopic") AND "complications". Potentially suitable studies were selected manually through inspection of title, abstract and full text. The basic eligibility criteria were: study investigated the GA in context of its power to predict postoperative complications, study is not a meta-analysis, review, editorial, comment or duplicate; work is available in English; study participants were aged ≥ 65 and were undergoing gastrointestinal surgery. The literature search was performed according to the PRISMA guidelines.[6] Two authors independently assessed risk of bias using the Newcastle-Ottawa Scale adapted to this subject.[7] Disagreement among the reviewers was discussed during a consensus meeting. The study was approved by the Ethics Committee of the Jagiellonian University. (No.1072.6120.319.2018/(20.12.2018)).

4. Results

4.1. Study selection

The detailed searching process is depicted in Figure 1. The two papers published by Kristjansson et al. analyzed the same population, however one of them focused on individual components of the GA[8] while the second investigated their combination.[9]

4.2. Study characteristics

The main characteristic of the 10 included studies is shown in Appendix Table 1. In total, 1940 patients (855 females and 1085 males; sample size 46–517 patients) were included. Minimal age for patients' inclusion was 65 years in three studies, 70 years in four and 75 years in the remaining three. The most common indication for surgery was for colorectal cancer alone, presented in six articles.[4–6,8–14] Three studies analyzed surgeries for various solid abdominal cancers.[15–17] One study investigated patients after laparoscopic cholecystectomy.[11]

Regarding the surgical technique, eight studies evaluated patients operated using both laparoscopic (10–81% of included patients) and open technique, while two investigated only laparoscopic operations.

Seven studies followed the patients up for 30-days,[4,8,11,12,14,16] one study for 90-days[17] and two for 1 year.[13,14] The postoperative morbidity was between 23.7% and 76.3% of patients in the given follow-up time period.

The detailed characteristics of the GA used in each study is presented in Table 1. Activities of Daily Living (ADL) or the Instrumental Activities of Daily Living (I-ADL), was used in 90% of studies, followed by the Geriatric Depression Score (80%), the Mini-Mental State Examination (70%), Polypharmacy (70%), the Mini Nutritional Assessment (MNA) (60%), the Charlson Comorbidity Index (50%), the Cumulative Illness Rating Scale (20%), the Blessed Orientation-Memory-Concentration score (10%) and the Clock Drawing Test (10%). Moreover, two authors used the Vitality Index (VI), which is used to assess the motivation of older patients with dementia towards daily living.[14,15] Samuelsson et al. analyzed the Downton fall risk index (DFRI)[13] and Fagard et al. the Mobility-Tiredness Test scale (MOB-T).[11] Two papers used the Nursing Delirium Screening Scale (NDSS)[5] and the Brief Fatigue Inventory (BFI).[17] No study reported the results for the test Short Physical Performance Battery (SPPB), the Timed Up and Go (TUG) and the Medical Outcomes Study Social Support Scale (MOS-SSS).

Three studies evaluated the GA as integrated score and used its cumulative result as a risk factor for postoperative complications. The presence of deficits in one or more[9,16] or two or more[11] GA domains were used as the cut-off and also a cumulative frailty definition.[9,11,16] Detailed results of these studies are presented in Table 2.

4.3. Functional domain

Nine included studies (90%) assessed preoperative physical function through the use of the ADL or the I-ADL scales. Kristjansson et al. used the Nottingham extended activities of daily leasing scale (NEADEL).[9] Five authors analyzed the usefulness of the functional domain in predicting postoperative complications. Three of them found that patients scoring as dependent in daily activities is strongly associated with increased risk of postoperative complications (Lee et al. OR 16.369 (1.233–217.2) p = 0.034; Fagard et al.; OR 0.39 (0.21–0.73) p = 0.006 and for the independent patients in the ADL; Meakawa et al. 1.2 (1.03–1.44); p = 0.0199).[4,12,15] Additionally, a deficit in the functional domain was shown to be a risk factor for postoperative delirium in the study by Maekawa et al. (ADL: OR 1.20 (1.03–1.44; p = 0.02; I-ADL: 1.46 (1.22-1.77); p < 0.01).[14] In case of the I-ADL and the NEADL, three out of four studies confirmed a significant predictive power.[4,8,15]

No study assessed the TUG and the SPPB or other scores requiring physical exercises.

4.4. Cognitive functioning

Cognitive functioning was measured in all papers. The most

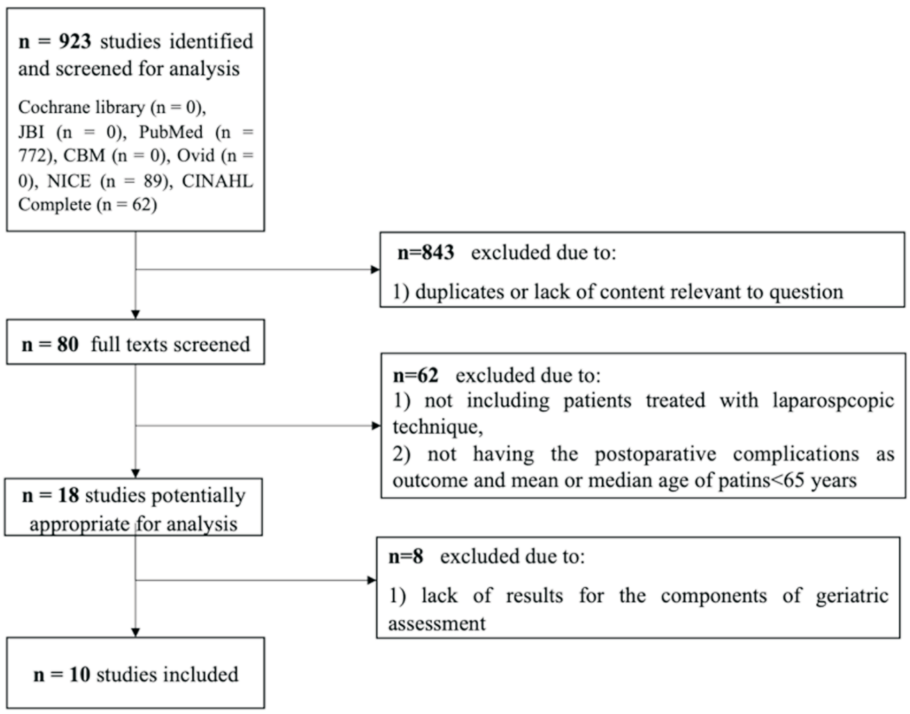

Figure 1. Search results and study selection.

Table 1
Individual components of GA and literature cut-off scores.

Study	Components of the GA associated with postoperative complications								Other domains
	Functional domain		Cognitive domain	Mood	Nutritional status	Physical function	Comorbidity	Polypharmacy	
	ADL (cut-off)	IADL (cut-off)	MMSE (cut-off)	GDS (cut-off)	MNA/MNA-SF (cut-off)	TUG SPPB (cut-off score)	CCI (cut-off score)	[drugs number]	
Nishizawa et al., 2017[14]	+ BI	+	+	+	-	–	–	-	VI
Lasithiotakis et al., 2013[16]	+ (< 5)	+ (< 8)	+ (< 21)	-	[MUST] (NR)	–	+ (≥ 3)	+ (> 5)	-
Samuelsson et al., 2019[13]	+ (< 5)	+ (NR)	+ (< 24)	+ [GDS-20] (> 5)	+ (< 11)	–	[ACCI] (> 9)	-	Fall risk (DFRI) Quality of life (EQ-5D)
Kenig et al., 2016[11]	+ (< 5)	+ (< 7)	BOMC (> 10) CDT (≤ 4)	+ (> 5)	+ (< 24)	–	–	+ (> 5)	–
Fagard et al., 2017[12]	+ (< 7)	+ (< 8)	+ (< 24)	+ (> 5)	+ (< 12)	–	+ (> 1)	+ (> 5)	Fatigue MOB-T
Lee et al., 2016[4]	+ (< 5)	+ (< 7)	+ (< 24)	+ [SGDS] (≥ 10)	+ (< 24)	–	+	+ (≥ 8)	Delirium risk (NDSS)
Maekawa et al., 2016[15]	+ BI (< 60)	+	+ (< 24)	+	-	–	–	–	VI
Badgwell et al., 2013[17]	-	+ (< 8)	Mini-Cog (> 2)	+ (> 4)	-	–	+ (≥ 3)	+ (yes/no)	Fatigue BFI
Kristjansson et al., 2010[8]	+ (< 19)	NEADL (< 44)	+ (< 24)	+ (< 13)	+ (< 17)	–	+ [CIRS]	+ (0–4, > 5)	–
Kristjansson et al., 2010[9]	+ (< 19)	NEADL (< 44)	+ (< 24)	+ (< 13)	+ (< 17)	–	+ [CIRS]	+ (< 5-fit, > 7-frail)	–
Number of studies reporting the domain	9/10 (90%)	10/10 (100%)	10/10 (100%)	9/10 (90%)	7/10 (70%)	0/10 (0%)	7/10 (70%)	7/10 (70%)	–

Abbreviations: BI, Barthel Index; VI, Vitality Index; ADL, activities of daily living; I-ADL, instrumental activities of daily living; MUST, malnutrition universal screening tool; MMSE, Mini-Mental State Examination; Mini-Cog test, GDS, geriatric depression score; GDS-20, geriatric depression score 20; GDS-15, geriatric depression score 15; SGDS, Korean geriatric depression score; MNA, Mini Nutrional Assessment; MNA-SF, Mini Nutrional Assessment short form; TUG, time up and go; SPPB, short physical performance battery; CCI, Charlson Comorbidity Index; CIRS, cumulative illness rating scale; DFRI, downton fall risk index; BOMC, Blessed Orientation-Memory-Concentration Test; CDT test, Clock Drawing Test; MOB-T, Mobility-Tiredness Test scale; NDSS, nursing delirium screeing scale; BFI, brief fatigue inventory; NEA DL, Nottingham extended acitities od daily leasing; ACCI, Age-adjusted Charlson Comorbidity Index; TRST, Triage Risk Screening Tool; ”yes”, there was polypharmacy; “no”, there was no polypharmacy; “–” there is no significant associations; NR, not reported.

Table 2
Studies analyzing the predictive effectiveness of the cumulative GA.

Study	Investigated combination of GA elements	Results	
		Postoperative complications	Postoperative delirium
Kenig et al., 2016[11]	ADL + I-ADL + GDS+MNA + polypharmacy + BOMC/CDT + CCI	Elective Patients: All complications: OR 1.2 (0.5–2.7; p = 0.63) Major complications: OR 0.89 (0.3–2.6; p = 0.84) Emergency Patients: OR 3.4 (1.2–9.7; p = 0.02)	NR
Lasithiotakis et al., 2013[16]	ADL + I-ADL + MMSE + CCI + polypharmacy + MUST	OR 6.0 (1.2–30.4; p = 0.026)	NR
Kristjansson et al., 2010[9]	ADL + I-ADL + GDS + MNA + MMSE + CIRS + polypharmacy	OR 3.13 (1.65–5.92; p < 0.05)	NR
Nishizawa et al., 2018[14]	ADL + I-ADL + MMSE + GDS + VI	NR	Low risk in CGA: 5% CLS, 10% c. SLS High risk in CGA: 60% CLS, 20% SLS p = 0.0153

Abbreviations: ADL, activities of daily living; I-ADL, instrumental activities of daily living; MMSE, Mini-Mental State Examination; MUST, malnutrition universal screening tool; GDS, geriatric depression score; MNA, Mini Nutrional Assessment; CCI, Charlson Comorbidity Index; CIRS, cumulative illness rating scale; BOMC, Blessed Orientation-Memory-Concentration Test; CDT test, Clock Drawing Test; OR, odds ratio; p, p-value; Cl, confidence interval; NR, not reported.

common evaluation tool was the Mini-Mental State Examination (MMSE) (80% of the studies) followed by the Mini-Cog,[17] the Clock Drawing Test (CDT) and the BOMC.[11] However, only five of them evaluated the predictive power and only one author confirmed its significance in predicting postoperative complications (Maekawa et al. OR 1.29 (1.21–1.39); p < 0.0001).[15]

4.5. Nutritional status

State of nutrition was analyzed by seven studies. Six studies used the full MNA score, one study applied the shortened form (SF-MNA) and Lasithiotakies et al. used the MUST scale.[16] The MNA turned to be insignificant in predicting postoperative complications, regardless of the subgroup analysis (short term complications,[5] severe complications[8,16] or frail patients[8,11]). Samuellson et al. showed borderline significance for the MNA-SF scale (OR 0.25 (0.06–1.02; $p = 0.05$).[13] Badgwell et al. observed that weight loss > 10% was a significant risk factor of prolonged hospital stay (OR 6.5 (1.43–29.76; $p = 0.03$).[16]

4.6. Comorbidity

Seven studies investigated association of comorbidities and postoperative complications. The applied tools were the Charlson Comorbidity Index (CCI) in six studies and the cumulative illness rating scale (CIRS) in two studies.[8,9] Samuelsson et al. used the age-adjusted CCI.[13] Two authors investigated the predictive power of comorbidity scores. Only one study found that severe comorbidity was associated with a significant increased risk of serious post-operative complications (OR 5.13 (1.92–13.66; $p = 0.0001$).[8]

4.7. Risk of depression

The presence of preoperative depression was studied in nine articles. The most common tool for the assessment was the GDS-15 (4 studies). One study applied the GDS-20,[13] one the GDS-30 and Lee et al. used the modified Korean GDS.[4] Five studies evaluated the predictive power of the GDS. Only two authors showed that abnormal scores were a significant risk factor for postoperative complications (Meakawa et al. HR 0.88 (0.82–0.94) $p < 0.0003$; Kristjansson et al. OR = 4.58 (1.25–16.84) $p = 0.02$).[8,15]

4.8. Polypharmacy

The number of drugs taken by patient on a daily basis was considered in seven studies. Only five papers presented the cut-offs (> 5 drugs,[7,11,13] 0–4 and > 5,[9] 0–7 and > 8.[4] Only Badgwell et al. reported that polypharmacy was a risk factor for postoperative complications (OR 2.4 (1.09–5.48; $p < 0.05$).[17]

4.9. The GA as unified predictive factor

There were three studies that used various domains of GA as one unified tool to predict postoperative outcome.[9,11,16] The papers and sets of tests are presented in Table 2 together with the results of the multivariate regression analysis. All authors confirmed the effectiveness of these tools in predicting postoperative complications (OR 3.1–6.0.[9,11,16] Moreover, Nishizawa et al. confirmed its usefulness in predicting postoperative delirium ($p < 0.001$).[14]

4.10. Quality Assessment

The results of the quality assessment can be found in Figure 2. Detailed results per study are listed in Appendix Table 2. The overall quality of the studies was good. In all included studies the methods of geriatric evaluation was sufficient to judge potential risk of bias. There were no studies with control group. Two studies had loss to follow-up rates over 10%,[8,17] while another five did not provide sufficient information to assess adequacy of follow-up.[4,9,14–16] There were no other quality concerns.

5. Discussion

Analyzing each domain alone, the reviewed studies revealed in some parts conflicting results. Only scoring as dependent in the functional domain can be recognized as a leading risk factor of post-operative complications in the evaluated population. However, this does not mean that the other domains are redundant. The reason is probably a high inter-study heterogeneity. The studies often did not include consecutive patients (or we do not have information on that), the minimum age for the inclusion differed between studies (65, 70, 75 years), the number of patients in each study differed (49–517), and patients were often in good health and with stable comorbidities (85% of ASA evaluated patients were ASA ≤ 2). Moreover, the interpretation of the results presented in this review requires highlighting of some aspects of research design and course. The authors used different tools to evaluate the same geriatric domain with various cut-offs. In some of the studies there was no adjustment for important confounding factors (severity and length of surgery, laboratory parameters, etc.).

In the study by Kenig et al., the effectiveness of the functional domain could not be evaluated due to low number of dependent patients.[11] The nutritional status was analyzed in 70% of the studies, showing no association between the nutrition level and the risk of postoperative complications in the older population after elective surgery. This contradicts the results of other studies and systematic reviews.[18] However, analyzing the basic characteristics of the included population, most of them had no evidence of severe malnutrition and had normal biochemical results indicating adequate nu-

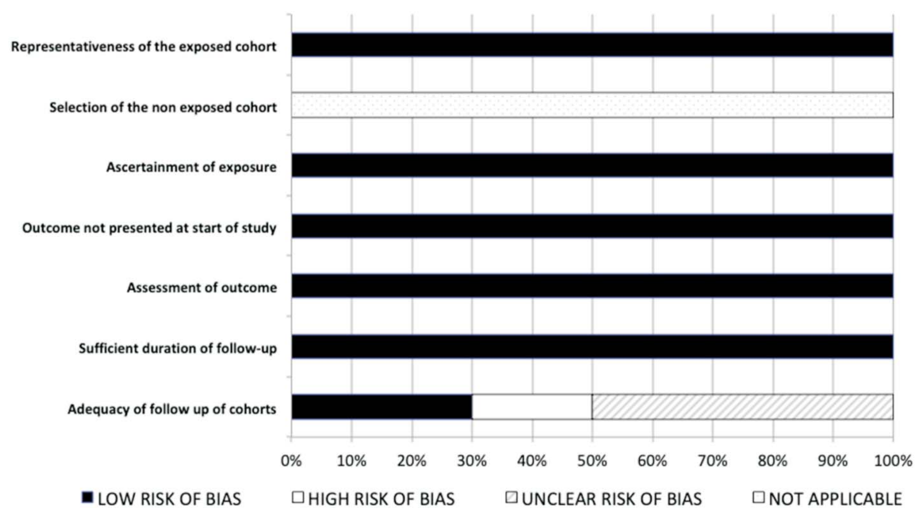

Figure 2. Quality assessment of the included studies.

trition. Thus, this could be one of the possible reasons why the authors did not report any association of the score with postoperative outcome. Considering the cognitive domain, intriguingly, despite laparoscopy being the dominant technique, the incidence of delirium in one study was 2–6 times higher than generally reported, which might have biased results of this study and lead to the overestimation of applicability of these scales;[14] or the delirium could have been underreported in other studies aiming to present postoperative complications in general and not only the delirium alone. In the case of assessment of comorbidities, Kristjansson et al. indicated that the CIRS scale was useful in predicting postoperative complications after colorectal cancer surgery. However, it was less effective than simple ECOG PS.[8,9] This could be due to the fact that the patients were optimally prepared for elective surgery with stable chronic diseases. It seems important to assess the comorbidity status as a part of individualized surgical treatment planning. However, as data regarding its significance are insufficient, and in many cases conflicting, patients with comorbidities should not be routinely considered as not fit enough for the surgical treatment. Closely related to presence of comorbidities is polypharmacy. Analysis of this factor revealed conflicting results with both very strong and no associations detected.[8,9,11] This could be due to large heterogeneity of the studies using many cut-offs or presenting only dichotomous results (yes/no),[17] making comparison difficult. None of the authors included the social domain, which has also previously been reported as a predictor of postoperative complications.[19] The same is in case of the TUG and the SPPB, which have shown to be strongly correlated with morbidity after surgery.[20]

The authors were however unanimous as to the effectiveness of a cumulative GA in predicting postoperative complications. Therefore, the preoperative evaluation should be performed as a cumulative assessment. It seems much more important to include a given domain of the GA than the choice of the specific tool or cut-off.

Strengths of our study is the systematic methodology to identify relevant articles in various databases, three investigators independently screened all articles with high level of agreement. Moreover, the review was not restricted to articles presenting the GA components but also, what seems more important, the importance of the cumulative GA.

The main limitation of this review was that included studies were heterogeneous in design, and study population. There was a great heterogeneity regarding the tumor stage, type and scope of the surgery. The studies also varied in number of included patients and GA tools used to evaluate the preoperative status of the patient. Another relevant point is that patients had already been qualified for the surgery by their physicians. Thus, majority of the analyzed patients can be qualified as fit to undergo surgery. Therefore, there is a great need for prospective, well-designed, multicenter studies using the same inclusion criteria, the same set of the GA tools and evaluating the outcome of the same type of surgery.

6. Conclusions

To predict the outcome of older patients after laparoscopic surgery it is recommended to perform a cumulative GA. However, the exact cut-offs for each domain and for a cumulative assessment have not been determined. For the individual domains (apart from the physical function) the results are too inconsistent to reach any clinical decision. This is mainly due to various bias associated with the included population and methodology of the studies analyzed. We need further prospective, well-designed studies investigating the usefulness of individual domains of GA, and cumulative scores, in predicting postoperative complications following laparoscopic surgery in older patients.

The disclosure section

The authors declare no conflict of interest.

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Appendix

Appendix Table 1
Characteristics of the included studies.

Study; year of publication	Study type and duration time	Minimal age for inclusion	Indication for surgery (% laparoscopic/ open/converted)	Total number of patients (female/male)	ASA/ECOG-PS (n = number of patients, NR- not reported)	Follow-up time and postoperative complications in %	Main aim	Main conclusion*
Yujiro Nishizawa et al., 2018[14]	Retrospective controlled clinical trial; 2009-2015	75	Colorectal cancer 100% (63%-single incision laparoscopy, 37% conventional laparoscopy)	134 (58/76)	ASA I = 10 (7%) II = 100 (75%) III = 24 (18%) ECOG-PS: NR	30 days 27.6% (including 19.4% of postoperative delirium)	Postoperative delirium	GA can indicate group of patients in higher risk of postoperative delirium.
Konstantinos Lasithiotakis et al., 2013[16]	Prospective cohort study; 2008-2011	65	Elective cholecystectomy (100% laparoscopic)	57 (29/28)	ASA I = 44 (77%) II = 11 (19%) III = 2 (4%) ECOG-PS: NR	30 days 23.7%	Postoperative complications	CGA is an important predictive factor for postoperative complications, LOS and pain a day after surgery (to the VAS scale).
Katja S. Samuelsson et al., 2019[13]	Prospective cohort study; 2010-2016	75	Colorectal cancer [O-90%/L-10%]	49 (26/23)	ASA II = 21(43%) III = 23(47%) IV = 5 (10%) ECOG-PS: NR	1 year 32.7%	Postoperative complications and length of hospital stay	There is no association between CGA and prolonged length of stay or postoperative complication after elective surgery for colorectal cancer.
Kenig et al., 2016[11]	Prospective cohort study; 2014-2015	65	Elective or emergency cholecystectomy [L-81%/O-16%/ C-3%]	126 (66/60)	ASA: I = 9 (7%) II = 73 (58%) III = 40 (32%) IV = 4 (3%) ECOG-PS: 0 = 24 (19%) I = 58 (47%) II = 24 (19%) III = 17 (13%) IV = 3 (2%)	30 days\10.6% elective surgery 36.7% emergency surgery	Postoperative complications	CGA is good predictor of postoperative complications and LOS in emergency settings.
Katleen Fagard et al., 2017[12]	Retrospective cohort study; 2009-2015	70	Colorectal cancer [O + C = 49% L = 51%]	190 (85/105)	ASA I = 3 (1.5%) II = 93 (49%) III = 93 (49%) IV = 1(0.5%)	30 days 44.7%-medical complications 20.0%-surgical complications	Postoperative complications	ADL is a predictor of postoperative complications in patients with high frailty level (according to G8 scale).
Yoon H. Lee et al., 2016[4]	Prospective cohort study; 2010-2014	70	Colorectal cancer [O-33.3%/ L-66.7%]	240 (102/138)	ASA I = 39 (16%) II = 174 (73%) III = 27 (11%)	30 days 76.3%	Postoperative complications	ADL and CCI are predictors of short-termed postoperative complications.
Yoshihiro Maekawa et al., 2016[15]	Prospective cohort study; 2005-2013	75	Various solid abdominal cancers [O-54.5%/ L-45.5%]	517 (166/351)	NR	1 year 24.0%-postoperative delirium	Postoperative delirium	I-ADL, GDS and MMSE are good predictors of postoperative delirium.
Brian Badgwell et al., 2013[17]	prospective	65	Various solid abdominal cancers [O-74%/L-26%]	111 (50-61)	ASA: < 2–91 ≥ 2–20 ECOG-PS: < 2–84 ≥ 2–27	90 days 48%	Postoperative complications	GA can help predict the need for discharge to a nursing facility or increased length of stay. Polypharmacy is predictor of prolonged LOS.
Siri R. Kristjansson et al., 2010[8]	prospective	70	Colorectal cancer [O-66%/L30%/ C-4%]	182 (104/78)	ASA: nr ECOG-PS 0 = 66 (36%) I = 62 (34%) II = 40 (22%) III = 14 (8%)	30 days 35.7%	Postoperative complications	ADL/IADL, CIRS and GDS scales are useful in predicting postoperative complications after colorectal cancer surgery. However, they are less effective than oncological scale ECOG PS.
Siri R. Kristjansson et al., 2010[9]	prospective	70	Colorectal cancer [O-66%/L-29%/ C-5%]	178 (102/76)	ASA I = 1 (0.5%) II = 81 (45.5%) III = 76 (43%) IV = 4 (2%) Missing = 16 (9%) ECOG-PS: NR	30 days 33%-fit patients 36%-intermediate patients 62%-frail patients	Postoperative complications	GA is predictor of early (within 30 days of surgery) postoperative complications.

Type of the operation: O, open; L, laparoscopic; C,converted; * GA, geriatric assessment; ADL, activities of daily living; LOS, length of stay; CCI, Charlson Comorbidity Index; MMSE, Mini-Mental State Examination; I-ADL, instrumental activits of daily living; GDS, geriatric depression score; ECOG PS, Eastern Cooperative Oncology Group Performance Status; CIRS, cumulative illness rating scale; ASA, American Society of Anesthesiologist Physical Status Classification System; NR, not reported.

Appendix Table 2
The detailed result of quality assessment of the included studies.

Publication	Selection			Outcome			
	Representativeness of the exposed cohort	Selection of the non exposed cohort	Ascertainment of exposure	Outcome not presented at start of study	Assessment of outcome	Sufficient duration of follow-up	Adequacy of follow up of cohorts
Yujiro Nishizawa et al., 2018[14]	1	NA	1	1	1	1	?
Konstantinos Lasithiotakis et al., 2013[16]	1	NA	1	1	1	1	?
Katja S. Samuelsson et al., 2019[13]	1	NA	1	1	1	1	1
Kenig et al., 2016[11]	1	NA	1	1	1	1	1
Katleen Fagard et al., 2017[12]	1	NA	1	1	1	1	1
Yoon H. Lee et al., 2016[4]	1	NA	1	1	1	1	?
Yoshihiro Maekawa et al., 2016[15]	1	NA	1	1	1	1	?
Brian Badgwell et al., 2013[17]	1	NA	1	1	1	1	0
Siri R. Kristjansson et al., 2010[8]	1	NA	1	1	1	1	0
Siri R. Kristjansson et al., 2010[9]	1	NA	1	1	1	1	?

Abbreviations: 1 point, low risk of bias; 0 point, high risk of bias; ?, unclear risk of bias; NA, not applicable.