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RESEARCH

Comparison Between Charlson Comorbidity Index (CCI) and The American Society of Anesthesiologists Physical Status Classification (ASA) in Predicting Mortality in Geriatric Patients Undergoing Anesthesia at Dr Sardjito Hospital Yogyakarta

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ABSTRACT

Background: Geriatric patients tend to have more comorbidities accompanied by a decline in physiological and cognitive function, which impacts perioperative outcomes. The combination of physiological dysfunction, especially changes in pharmacodynamics and pharmacokinetics of drugs, leads to several challenges in administering anesthesia. The Charlson Comorbidity Index (CCI) has been used to predict mortality based on comorbidity assessment. The American Society of Anesthesiologists (ASA) categorizes physiological status to estimate patient health based on anesthesia expert assessment. Increased CCI and ASA scores are known to have significant correlation to increased mortality in geriatric patients undergoing surgery.
Objective: To compare the Charlson Comorbidity Index (CCI) and the American Society of Anesthesiologists (ASA) Physical Status Classification in predicting mortality in geriatric patients undergoing anesthesia at Dr. Sardjito Hospital, Yogyakarta.
Methods: A retrospective observational study was conducted on all geriatric patients undergoing anesthesia procedures in the operating room of Dr. Sardjito Hospital, Yogyakarta, during the period of February-April 2021. Normality tests were performed using Kolmogorov-Smirnov. Bivariate analysis was conducted using the Chi-square test. A p-value of <0.05 was considered statistically significant. The predictive validity of CCI and ASA scores, as well as the optimal cutoff point for CCI scores, were evaluated using multivariate logistic regression analysis based on discrimination testing by observing the Area Under Curve (AUC) and the Hosmer-Lemeshow calibration test.
Results: There was a significant association between CCI scores and mortality (OR 4.589; 95% CI 1.257-16.747; p=0.021). Meanwhile, no significant association was found between ASA and mortality in geriatric patients undergoing anesthesia at Dr. Sardjito Hospital, Yogyakarta. The ROC curve showed an optimal cutoff point for CCI scores of 2.5 with a sensitivity of 26.7% and specificity of 90.6% (AUC 57.6%, p=0.321, 95% CI 0.409-0.744).
Conclusion: There is a significant association between increased CCI scores and mortality in geriatric patients. Meanwhile, no significant association was found between ASA and mortality in geriatric patients undergoing anesthesia at Dr. Sardjito Hospital, Yogyakarta

Keywords: Geriatrics, anesthesia, Charlson Comorbidity Index (CCI), American Society of Anesthesiologists (ASA)

INTRODUCTION

The term geriatrics was first documented in 5000 BC in ancient Indian medical texts, interpreted as premature aging.[1] Conventionally, geriatrics is defined as chronological age ≥ 65 years, with 65-74 years referred to as early geriatrics and >74 years as late geriatrics.[2] According to Law Number 13 of 1998, the elderly are defined as individuals aged 60 years and above.[3] In 2020, an estimated 727 million people worldwide were aged >65 years. This number is projected to double by 2050.[4] In Indonesia alone, the percentage of elderly individuals in 2020 doubled compared to 1971.[3]

As medical science advances, the geriatric population also increases due to higher life expectancy and decreased mortality rates. However, an increasing proportion of geriatric patients also receive healthcare services, including anesthesia and intensive therapy.[3,5] In 2006, in the United States, 50% of ICU patients were geriatric. The issue is not only related to the increasing population but also to the rising costs. It is known that in the United States, ICU care costs account for 25% of the total medical services provided.[6]

As age increases, physiological functions also decline, making individuals more susceptible to illness.[1] Changes in the nervous system can result in cognitive impairment, cardiovascular system changes such as increased blood pressure and decreased cardiac output, respiratory system changes such as decreased arterial oxygen saturation, gastrointestinal system changes such as delayed gastric emptying due to decreased hepatic metabolism, and renal system changes such as decreased glomerular filtration rate.

These physiological changes also affect the pharmacodynamics and pharmacokinetics of drugs, which need to be considered in the treatment of geriatric patients. Geriatric patients tend to have more comorbidities accompanied by a decline in physiological and cognitive function, affecting perioperative outcomes.[5,7] This also applies during anesthesia administration. The combination of physiological dysfunction, especially changes in pharmacodynamics and pharmacokinetics of drugs, poses several challenges in anesthesia administration.[8]

The American Society of Anesthesiologists (ASA) developed a classification system to estimate patient health status based on anesthesia expert assessment. The ASA score consists of a six-point scale, with a score of 1 representing a healthy patient and a score of 6 representing a deceased patient based on comorbidities, history of trauma, obesity, smoking status, alcohol consumption, and the need for surgery.[9] The application of the ASA score is commonly done in the elderly population undergoing surgery, especially in orthopedic trauma cases. A total ASA score ≥3 is found to be associated with a higher risk of mortality. The ASA score also serves as a predictor for postoperative complications and readmission risk.[10]

The Charlson Comorbidity Index (CCI) has been used to predict mortality based on comorbidity assessment. The CCI score consists of 19 points related to mortality, with a total score of 33 to estimate the probability of death within one year. Unlike ASA, CCI involves objective assessments to evaluate systemic and local diseases with adjustments based on age. The CCI score has been used in hospitals as a prognostic indicator to assess 30-day, 90-day, and 1-year mortality rates in elective surgery and breast cancer patients.[11] Previous studies have also reported that CCI is a significant predictor for assessing 30-day postoperative complications and one-year mortality in the elderly population.[12]

Both ASA and CCI scores are used to evaluate patient health status and mortality risk. However, the main difference between ASA and CCI is that ASA provides an estimate of the patient's overall health condition during surgery, while CCI describes the history of specific disease comorbidities.[13] The ASA score is a simple patient evaluation tool that can be quickly used by anesthesiologists, but its use in predicting mortality needs to be evaluated to determine if it is comparable to CCI. The CCI score provides a more detailed assessment, while the ASA score is easier to use compared to the CCI score, which requires extensive calculations. Comparing the predictive strength of CCI and ASA scores for mortality is intriguing considering the differences in accessibility and components of these two scores.[14] Therefore, this study aims to determine the comparison between the Charlson Comorbidity Index (CCI) and the American Society of Anesthesiologists (ASA) Physical Status Classification in predicting mortality in geriatric patients undergoing anesthesia at Dr. Sardjito Hospital.

METHODS

This study is a retrospective observational study on geriatric patients undergoing anesthesia at Dr. Sardjito Hospital. It is part of a multicenter study titled "Anesthesia and Intensive Therapy Services Profile for Geriatric Patients in Indonesia: A Study on Characteristics, Management, and Outcomes," conducted by the College of Anesthesiology and Intensive Therapy at 14 Hospitals in Indonesia under ethical approval number KE/FK/1381/EC/2020. Sampling was done using total sampling method on all geriatric patients undergoing surgery at Dr. Sardjito Hospital, Yogyakarta, during the period of February-April 2021 who meet the inclusion and exclusion criteria. Data collected included patient history, physical examination results, and secondary data from the medical records of Dr. Sardjito Hospital, Yogyakarta. Inclusion criteria were patients aged 60 years or older undergoing anesthesia at Dr. Sardjito Hospital, Yogyakarta. Exclusion criteria were patients with incomplete medical records and without permission from the hospital.

Drop-out criteria were the absence of or incomplete medical records that could not be evaluated. All data were analyzed using SPSS version 26.0. Categorical data were expressed in frequency and percentage, while numerical data were expressed as median due to non-normal distribution. Normality test was performed using Kolmogorov-Smirnov. Bivariate analysis was conducted using the Chi-square test. The predictive validity of ASA and CCI scores was evaluated using multivariate logistic regression analysis ($p < 0.25$), and discrimination was assessed by the Area Under the Curve (AUC) along with the Hosmer-Lemeshow calibration test. A p-value of <0.05 was considered statistically significant. The optimal cutoff point for CCI scores was assessed based on the ROC curve and Youden's index.

RESULT

The characteristics of the study subjects were analyzed based on demographic data including age, gender, body weight, height, body mass index, CCI score, ASA classification, comorbidities, type of surgery, type of anesthesia, events in the operating room, and events in the recovery room. Of the 239 subjects, the median age of the patients was 65 years, consisting of 133 males (55.6%) and 106 females (44.4%), with a BMI of 22 kg/m2 and a median weight of 55 kg and height of 155 cm.

The most common comorbidity among patients was tumor, present in 39 patients (16.3%). The most common types of surgeries performed were oncological surgeries (65 individuals, 27.2%), followed by ophthalmology (40 individuals, 16.7%), and digestive surgeries (n=28, 11.7%). The majority of patients had a CCI score of 0 (n=167, 69.9%) and ASA classification II (n=227, 95%), and received general anesthesia (n=185, 77.4%). The most common complications occurring in the operating room and recovery room were hypotension (n=28, 11.7%; n=7, 2.9%), and there were 15 geriatric patients (6.3%) who died within 30 days after anesthesia. Patient demographic data can be seen in Table 1.

The optimal cutoff point for the CCI score obtained from the analysis of this study is 2.5 with a sensitivity of 26.7% and a specificity of 90.6% (Table 4). However, since the CCI score is an integer, the cutoff point used is 3. Furthermore, the Hosmer-Lemeshow calibration test indicates that the Charlson Comorbidity Index (CCI) can predict the prognosis of geriatric patients undergoing anesthesia procedures (chi-square = 0.828 and p = 0.991). The CCI score shows very weak discrimination value (AUC 57.6%, p = 0.321, 95% CI 0.409-0.744) with good calibration (Hosmer-Lemeshow p = 0.987) towards 30-day mortality in geriatric anesthesia patients.

This is similar to ASA, which shows very weak discrimination value (AUC 51.5%, p =

Table 1. Demographic Data

Characteristics	Median (minimum-maximum) or n(%)
Age, years	65 (60-94)
Gender	
Male	133 (55.6)
Female	106 (44.4)
Body weight, kg	55 (30-85)
Height, cm	155 (135-178)
Body mass index, kg/m ^{2}	22 (13-33)
CCI Score[a]	
Score <3	220 (92)
Score ≥3	19 (8)
ASA classification	
ASA I-II	227 (95)
ASA III-VI	12 (5)
Comorbid	
Myocardium infarction	5 (2,1)
Congestive heart disease	17 (7.1)
Peripheral vascular disease	17 (7.1)
Cerebrovascular disease	7 (2.9)
Dementia	3 (1.3)
COPD	3 (1,3)
Mid liver disease	1 (0.4)
Moderate-severe liver disease	2 (0.8)
Diabetes mellitus	37 (15.5)
Hemiplegia	1 (0.4)
Moderate-severe kidney disease	12 (5)
Tumor	39 (16.3)
Leukemia	1 (0.4)
Lymphoma	1 (0.4)
Metastatic tumor	3 (1,3)
Surgery types	
Trauma	3 (1,3)
Oncology	65 (27.2)
Digestive	28 (11.7)
Obstetrics	1 (0.4)
Gynecology	19 (7.9)
Neurology	7 (2.9)
Ophthalmology	40 (16.7)
Orthopedics	25 (10.5)
ENT	6 (2.5)
Plastic Surgery	4 (1.7)
Urology	11 (4.6)
Vascular	3 (1,3)
Non-operative/procedural sedation	27 (11.3)
Anesthesia types	
General anesthesia	185 (77.4)
Regional anesthesia	
Spinal anesthesia	51 (21.3)
Epidural anesthesia	24 (10)
Peripheral nerve block	2 (0.8)
Operating room events	
Hypotension	28 (11.7)
Bleeding exceeding EBV	1 (0.4)
Awake durante	2 (0.8)
Surgery duration exceeds	2 (0.8)
prediction	1 (0.4)
Anesthesia procedure	6 (2.5)
conversion	
Others	
Events in recovery room	
Hypotension	7 (2.9)
Bleeding exceeding EBV	3 (1,3)
Delayed emergence	1 (0.4)
Shivering	1 (0.4)
PONV	1 (0.4)
Painful	1 (0.4)

CCI = Charlson Comorbidity Index; ASA = American Society Anesthesiology

Table 2. AUC Values of CCI as a Predictor of Mortality in Geriatric Patients Undergoing Anesthesia

Parameter	AUC	P	95%CI
CCI	0.576	0.321	0.409-0.744

Table 3. AUC Values of ASA as a Predictor of Mortality in Geriatric Patients Undergoing Anesthesia

Parameter	AUC	P	95%CI
ASA	0.515	0.846	0.364-0.666

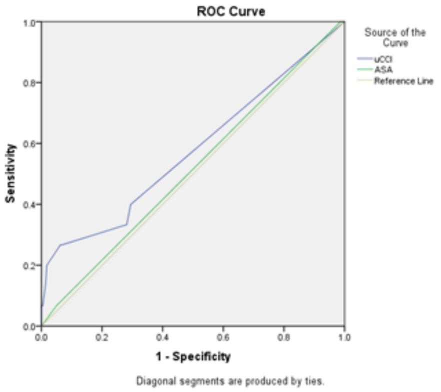

Figure 1. ROC Curve Comparison of CCI and ASA as Mortality Predictors

0.846, 95% CI 0.364-0.666) towards 30-day mortality in geriatric anesthesia patients.

Based on the bivariate analysis of factors influencing mortality (Table 5), a significant relationship ($p < 0.05$) was found between mortality and age (p=0.030) and Charlson's Comorbidity Index (CCI) score (p=0.022).

Variables with $p < 0.25$ were identified, including age, gender, and CCI, and analyzed multivariately to determine which variables had a greater impact on mortality. The results of the multivariate analysis in Table 6 indicate that age and CCI score are independently associated

Table 4. Sensitivity, Specificity, and Youden's Index Based on ROC Curve

Cut-Off score	Sensitivity	Spesificity	Youden's Index
-1,0	1,000	0,000	0,000
0,5	0,533	0,504	0,038
1,5	0,400	0,746	0,146
2,5	0,267	0,906	0,173
3,5	0,200	0,960	0,160
4,5	0,133	0,982	0,115
5,5	0,067	0,991	0,058
7,5	0,067	0,996	0,062
10,0	0,000	1,000	0,000

Table 5. Bivariate Analysis of Mortality in Geriatric Patients Undergoing Anesthesia

Variable	Mortality Yes n (%)	Mortality No n (%)	P
Age			
60-69 years old	7 (2.9)	168 (70.3)	0.030*
≥ 70 years old	8 (3.3)	56 (23.4)	
Gender			
Male	7 (2.9)	126 (52.7)	0.23
Female	8 (3.3)	98 (41)	
CCI			
< 3 points	11 (4.6)	209 (87.4)	0.022*
≥ 3 points	4 (1.7)	15 (6.3)	
ASA classification			
ASA I-II	14 (5.9)	213(89.1)	0.518
ASA III-VI	1 (0.4)	11 (4.6)	
Surgery type			
Low-moderate risk	8 (3.3)	131 (54.8)	0.696
High risk	7 (2.9)	93 (38.9)	
Anesthesia type			
General anesthesia	11 (4.6)	174 (72.8)	0.750
Regional anesthesia	4 (1.7)	50 (20.9)	

CCI = Charlson Comorbidity Index; ASA = American Society Anesthesiology; *statistically significant (p<0,05)

Table 6. Multivariate analysis of mortality in geriatric patients undergoing anesthesia

Variable	P	OR	95% CI
Age	0.036*	3.181	1.081-9.366
Gender	0.559	1.380	0.468-4.065
CCI ≥3	0.021*	4.589	1.257-16.747

CCI = Charlson Comorbidity Index; *statistically significant (p<0,05)

with mortality in geriatric patients undergoing anesthesia, with higher age (OR 3.181; 95%CI 1.081-9.366; p=0.036) and CCI score (OR 4.589; 95%CI 1.257-16.747; p=0.021) increasing the risk of mortality in geriatric patients undergoing anesthesia.

DISCUSSION

In this study, the demographic characteristics of geriatric patients undergoing anesthesia at Dr. Sardjito Hospital in Yogyakarta were predominantly male, with an average age of 65 years and a BMI of 22 kg/m2. The research indicates a significant correlation between age and mortality, where patients aged ≥70 years are at a threefold higher risk. This is supported by previous studies showing a significant correlation between increased mortality, prolonged duration of surgery, and age, especially among patients aged ≥85 years, with a significant impact on longer surgery durations.[15]

Pneumonia aspiration is one of the causes of death in geriatric anesthesia patients. When compared to patients aged 60 or 70 years, those aged 80 years and ≥90 years are at nearly 1.6 and 2.3 times higher risk of pneumonia aspiration, respectively. Male patients are three times more likely to develop pneumonia aspiration than females. This may be due to the increased distance between the hyoid bone and mandible with advancing age in males compared to females.[16] The change in hyoid bone position indicates atrophy of the surrounding muscles, narrowing the space in the larynx, thus interfering with the physiological swallowing movement, which can lead to pneumonia aspiration and death.[17]

Regarding patient comorbidities, most patients have comorbidities such as tumors or malignancies (16.3%), diabetes mellitus (15.5%), congestive heart failure (7.1%), and peripheral vascular disease or peripheral arterial disease (7.1%). Malignancy is closely associated with the aging process, with its prevalence increasing with age.

Older age is associated with an increased prevalence of chronic diseases, conditions related to aging (geriatric syndrome), and weakness.[18] Prolonged exposure to carcinogenic agents, accumulation of DNA damage, defects in tumor suppressor genes, disturbances in cell repair mechanisms, oncogenic activation, and weakened immunity are considered responsible for the high incidence of cancer in older individuals. Because carcinogenesis is a very lengthy process, the incidence of cancer in older age is a natural event.[19,20] Prospective cohort studies said that in geriatric patients undergoing therapeutic sedation, most deaths are due to cancer (84%). The mortality rate from cancer is 12% for non-metastatic solid tumors in six months, and 45% for metastatic solid tumors. The mortality rate from cancer in three years is 34% for non-metastatic tumors, and 83% for metastatic tumors.[21]

Diabetes is a leading cause of morbidity and mortality in geriatric patients, mostly due to macrovascular complications. Age and weight are risk factors for diabetes. During the aging process, there is an increase in fasting plasma glucose by 2 mg/dL per decade, so elderly patients at higher risk of developing diabetes. Weight gain and loss of muscle mass are often observed with advancing age, resulting in worsening insulin resistance at the muscle and fat levels. Therefore, beta-cell function is affected not only by age-related functional impairment but also by worsening insulin resistance. Additionally, in the elderly, there are often comorbidities, decreased activity, and medications that can exacerbate insulin resistance.[22]

The risk of postoperative mortality increases in patients with preoperative cardiac comorbidities.[23] In hospital mortality evaluations, a history of myocardial infarction and congestive heart failure are predictive factors of in-hospital mortality.[24] Congestive heart failure is significantly associated with mortality, as this condition induces monocytes to produce more tumor necrosis factor-alpha (TNF-alpha) and less interleukin-10, leading to weakened immune system.[25]

Peripheral arterial disease (PAD) rarely occurs in younger populations. The prevalence of PAD increases with age, with over 20% of people over 80 years old suffering from PAD.[26,27] Patients with PAD have a higher risk of all-cause mortality, cardiovascular mortality, and cardiovascular events. In a 10-year follow-up study of 565 patients with an average age of 66 years old, PAD significantly increased the risk of all-cause mortality (RR=3.1), death from cardiovascular disease (RR=5.9), and death from coronary artery disease (RR=6.6).[28] Peripheral vascular disease is caused by the development of atherosclerotic disease leading to macro and microvascular dysfunction through a complex inflammatory response mechanism involving various blood vessel cells, thrombotic factors, cholesterol, and inflammatory molecules.[27]

Geriatric patients mostly undergo oncologic (27.2%), ophthalmologic (16.7%), and digestive (11.7%) surgeries. Cohort studies show a significant increase in mortality rates in patients aged ≥65 years undergoing digestive surgery with six mortality risk factors in geriatric patients including age ≥85 years (OR, 2.62; 95% CI, 1.08-6.31; P = 0.032), emergency surgery (OR, 3.42; 95% CI, 1.67-6.99; P = 0.001), anemia (OR, 1.80; 95% CI, 1.02-3.17; P = 0.041), white blood cell count > 10,000/mm³ (OR, 1.90; 95% CI, 1.08-3.35; P = 0.024), ASA class IV (OR, 9.86; 95% CI, 1.77-54.7; P = 0.009), and oncologic surgery (OR, 4.03; 95% CI, 1.99-8.19; P <0.001).[29] Another cohort study shows a mortality rate of 22% in geriatric patients undergoing digestive surgery. Several factors analyzed were found to significantly increase mortality rates, including ASA grades IV-V, duration between symptom onset and time of surgery, conditions allowing only palliative surgery (gastrointestinal bypass, colostomy), or without surgical intervention (non-therapeutic laparotomy), such as advanced-stage mesenteric vascular disease or complex gastrointestinal malignancies.[30]

General anesthesia is the most frequently used anesthesia procedure in geriatric patients (n=185, 77.4%). There was no significant difference between general and local anesthesia regarding mortality in this study. Previous studies have suggested that general anesthesia has a higher incidence of pulmonary complications and mortality compared to local anesthesia.[31–33] However, recent retrospective studies have shown no significant difference between general and local anesthesia regarding pulmonary complications or mortality.[17,23,34,35]

The most common complication occurring in the operating room and recovery room is hypotension (11.7%). Geriatric patients with intraoperative mean arterial pressure (MAP) lower than 65 mmHg are significantly associated with postoperative mortality, with an AUC value of 0.850, indicating that this clinical indicator is highly useful in predicting postoperative mortality in geriatric patients. Intraoperative hypotension is caused by vasodilation and decreased peripheral vascular resistance due to circulatory inhibition after anesthesia induction.[36]

Meta-analysis studies have shown that intraoperative hypotension is associated with increased risk of postoperative acute kidney injury, myocardial injury, and 30-day mortality in non-cardiac surgery, and suggest that intraoperative MAP should not be below 60 mmHg.[37] Another study indicates that a duration of MAP <49 mmHg for more than 5 minutes can increase 30-day mortality outcomes in non-cardiac surgery.[38] This may be due to the geriatric patients' vasculature being more fragile and experiencing a decrease in the ability to self-regulate. Kidney blood flow and glomerular filtration rate can remain stable when MAP is in the range of 75-170 mmHg, but this will depend on blood pressure when MAP is outside this range.[39]

Geriatric patients undergoing craniotomy surgery for brain tumor resection experienced bleeding one day after surgery. Laboratory results showed decreased fibrinogen and increased fibrin degradation such as d-dimers, indicating disseminated intravascular coagulation (DIC) condition. The formation of DIC after craniotomy following brain tumor resection is one of the severe complications where almost half of the patients in reported cases died after surgery.[40,41]

This study shows a significant relationship between CCI score (≥3) and mortality of patients 30 days after anesthesia procedure ($p=0.021$, $OR=4.589$). Meanwhile, no significant relationship was found between ASA classification and mortality ($p=0.518>0.05$). This finding is consistent with previous studies, which demonstrated that an increase in the CCI score is associated with higher mortality rates, whereas ASA classification is not significantly associated with mortality.[42] CCI score (HR=1.132; 95% CI 1.009–1.270; $p=0.035$) is a significant predictor of death.[42] Studies on geriatric patients undergoing emergency abdominal surgery show that CCI ≥4 has lower survival rates. An increase in CCI by 1 point correlates with a 16.9% increase in surgical mortality.[43] Research on geriatric patients undergoing femur fracture surgery found that CCI score is significantly associated with in-hospital mortality ($p=0.031$), 30-day mortality ($p=0.010$), and 1-year mortality ($p<0.001$).[44] A meta-analysis involving 544,733 participants showed increased mortality in patients with high ASA classification and Charlson Comorbidity Index (CCI) scores. ASA classification and CCI score are important risk factors and have the same predictive ability for geriatric patient mortality.[14,23,46]

Approximately 85% of geriatric patients undergoing femur surgery who had ASA classification III-IV died within 30 days.[47] It was found that ASA III or higher was associated with high mortality rates, with the highest mortality risk being ASA IV-V at 3.8 times and CCI score >4 at 3.6 times the risk of 12-month mortality.[48,49] ASA classification has a significant association with mortality; ASA III is at 2.5 times higher risk and ASA IV is at nearly 5 times higher risk compared to ASA I-II.[50] In trauma cases, it was found that CCI score and ASA classification are related and can predict each other's score. A CCI score of zero is predictive of ASA I or II, CCI 1-2 is predictive of ASA III or IV, and CCI ≥3 is predictive of ASA IV.[51] CCI score provides a more detailed assessment compared to ASA classification. However, obtaining data and calculating CCI score can be time-consuming, so ASA classification is more often used in predicting mortality. Additionally, health status and lifestyle factors such as smoking and obesity that may correlate with mortality are considered in ASA classification but not in CCI score.[14,23]

This study has several limitations. First, retrospective review of medical records is prone to coding errors and data recording. Second, this study does not know the history of illness, hospitalization history, and history of previous surgery or anesthesia of patients in other hospitals as it only involves one hospital center. Despite these limitations, this study was able to answer important questions regarding the comparison of CCI and ASA scores in predicting mortality in geriatric patients undergoing anesthesia procedures.

CONCLUSION

This study indicates that CCI has a significant association with mortality in geriatric patients undergoing anesthesia procedures at RSUP Dr. Sardjito Yogyakarta. Meanwhile, no significant relationship was found between ASA and mortality in geriatric patients undergoing anesthesia procedures at RSUP Dr. Sardjito Yogyakarta.

RECOMMENDATION

It is necessary to involve larger population such as doing multicenter study and extend the duration of sample collection to within 1 year or 5 years so that this can provide more accurate results and significant differences among each variable.

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