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Investigation of the relationship between prolonged ventilation and the Glasgow Prognostic Score after elective isolated coronary bypass surgeries in advanced-age patients

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ABSTRACT

Objectives: Coronary artery bypass graft (CABG) surgeries are the most beneficial treatment method for atherosclerotic heart disease. Prolonged ventilation is a significant condition that poses risks such as infection, renal failure, prolongs hospital stays, and increases treatment costs. In this current study, we aimed to reveal the relationship between prolonged mechanical ventilation and Glasgow Prognostic Score (GPS), in patients aged 65 years and older who underwent isolated CABG.

Methods: Patients aged 65 years and over who underwent elective isolated coronary bypass surgery with cardiopulmonary bypass in our clinic, between June 2017 and June 2022, were included in the study retrospectively. The patients who were extubated within eight hours of the surgeries were determined as Group 1, whereas those who were extubated after 8 hours were determined as Group 2.

Results: Prolonged ventilation occurred in 101 (20.7%) patients (Group 2). The median age of the 385 patients included in Group 1 and 101 patients in Group 2 was 68 (66 to 91) and 71 (66 to 88) years, respectively (p = 0.216). The two groups were similar in regards to gender, hypertension, smoking, diabetes mellitus, body mass index, history of cerebrovascular accident and left ventricular ejection fraction rates. In the multivariate analysis, left ventricular ejection fraction < 35% (OR: 1.136, 95% CI: 1.065-1.652, p = 0.029), total perfusion time (OR: 1.190, 95% CI: 1.040-1.659, p = 0.012), and GPS = 2 (OR: 1.479, 95% CI: 1.130-2.169, p = 0.004) were determined as independent predictors for prolonged ventilation.

Conclusions: GPS value calculated preoperatively in elderly patients is a parameter that indicates the increased ventilation need. With the GPS score evaluation, patient groups at risk for prolonged ventilation may be identified and necessary precautions may be undertaken.

Keywords: Glasgow Prognostic Score, coronary artery bypass graft, morbidity, postoperative term, prolonged ventilation

Coronary artery bypass graft (CABG) surgeries are the most beneficial treatment method for atherosclerotic heart disease and at present, they are carried out with high success rates [1]. However, despite the

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advances in surgical techniques, various undesirable difficulties may occur after these operations [2]. One of the most important of these is the inability to end ventilation at the scheduled time for patients operated on stably, under elective conditions.

Currently, most patients are removed from ventilation within the first 6 to 8 hours after these operations. Extubation failure is one of the most common complications in the first 24 hours in these patients. In general, not being able to wean from ventilation within the first 8 hours is considered prolonged ventilation, though some studies have established this threshold at 6 hours [3]. The need for ventilation for more than 24 hours is seen with a frequency of 5 to 10% after isolated CABG operations [4]. It is significant that poses risks such as infection, and renal failure, prolongs hospital stays, and increases treatment costs [4, 5]. The risk is increased in elderly patients and those with lung disease [5]. For this reason, in many cardiovascular centers, attention is paid to extubating patients as early as possible with appropriate anesthesia applications [6].

In various studies, low albumin and high C-reactive protein (CRP) levels have been shown in cardiovascular diseases and undesirable events after CABG surgeries [7-9]. In another study, low albumin and high C-reactive protein were shown to be associated with prolonged mechanical ventilation times in patients intubated in the intensive care unit [10]. The Glasgow Prognostic Score (GPS) is a parameter determined by albumin and CRP values, and it is associated with poor postoperative clinical outcomes after transcatheter aortic valve replacement [11]. In this current study, we aimed to reveal the relationship between prolonged mechanical ventilation and GPS, in patients aged 65 years and older who underwent isolated CABG.

METHODS

Patients aged 65 years and over who underwent elective isolated coronary bypass surgery with cardiopulmonary bypass (CPB) in our clinic, between June 2017 and June 2022, were included in the study retrospectively. A total of 908 CABG operations were performed in patients aged 65 years and over within the study dates. All operations were performed by the same surgical team, and the inten-sive care management of the patients was also carried out by the same team. Intubated emergency surgeries or those performed under oxygen support, patients with critical preoperative condition (positive inotropic support or intra-aortic balloon support), patients with intraoperative mortality, patients undergoing combined surgeries, those with renal or hepatic insufficiency, those with pulmonary infection in the last month, as well as patients who were re-explored within the first 8 hours after the operation, were all excluded from the study. Following the application of the exclusion criteria, 486 consecutive patients were included in the study. The patients were divided into two groups according to the duration of postoperative ventilation. Accordingly, the patients who were extubated in the cardiovas-cular surgery intensive care unit within eight hours of the surgeries were determined as group 1, whereas those who were extubated after 8 hours were determined as Group 2. There were 385 patients in group 1, and 101 patients in Group 2 (Fig. 1).The demographic characteristics of the patients, preoperative hemogram (white blood cell, hematocrit, thrombocyte), biochemistry (urea, creatinine, C-reactive protein), echocardiography (left ventricular ejection fraction), intraoperative perfusion times, post-operative blood product transfusions, positive inotropic needs and ventilation times were recorded.

Glasgow Prognostic Score (GPS)

In the GPS evaluation, the C reactive protein value is above 10 mg/L and the albumin value is below 35 g/L. If both of these conditions are present the score is 2, if only one of them is present, the score is 1 and in the absence of both conditions, the score is evaluated as 0 [11].

Anesthesia Technique and Surgical Procedure

General anesthesia was used during all procedures. Following intravenous midazolam administration (0.05–0.1 mg/kg; Zolamid®; Defarma, Turkey), invasive catheterization of the radial artery was carried out. Patients were then observed, thereafter fentanyl (Talinat®, Vem, Turkey) and pentothal (Pental® Sodium, Turkey) were used to induce anesthesia in all patients. Rocuronium bromide (Curon®, Mustafa Nevzat, Turkey) was administered to aid endotracheal intubation. To maintain anesthesia, sevoflurane (Sevorane®, Abbvie, Turkey) was combined with a mixture

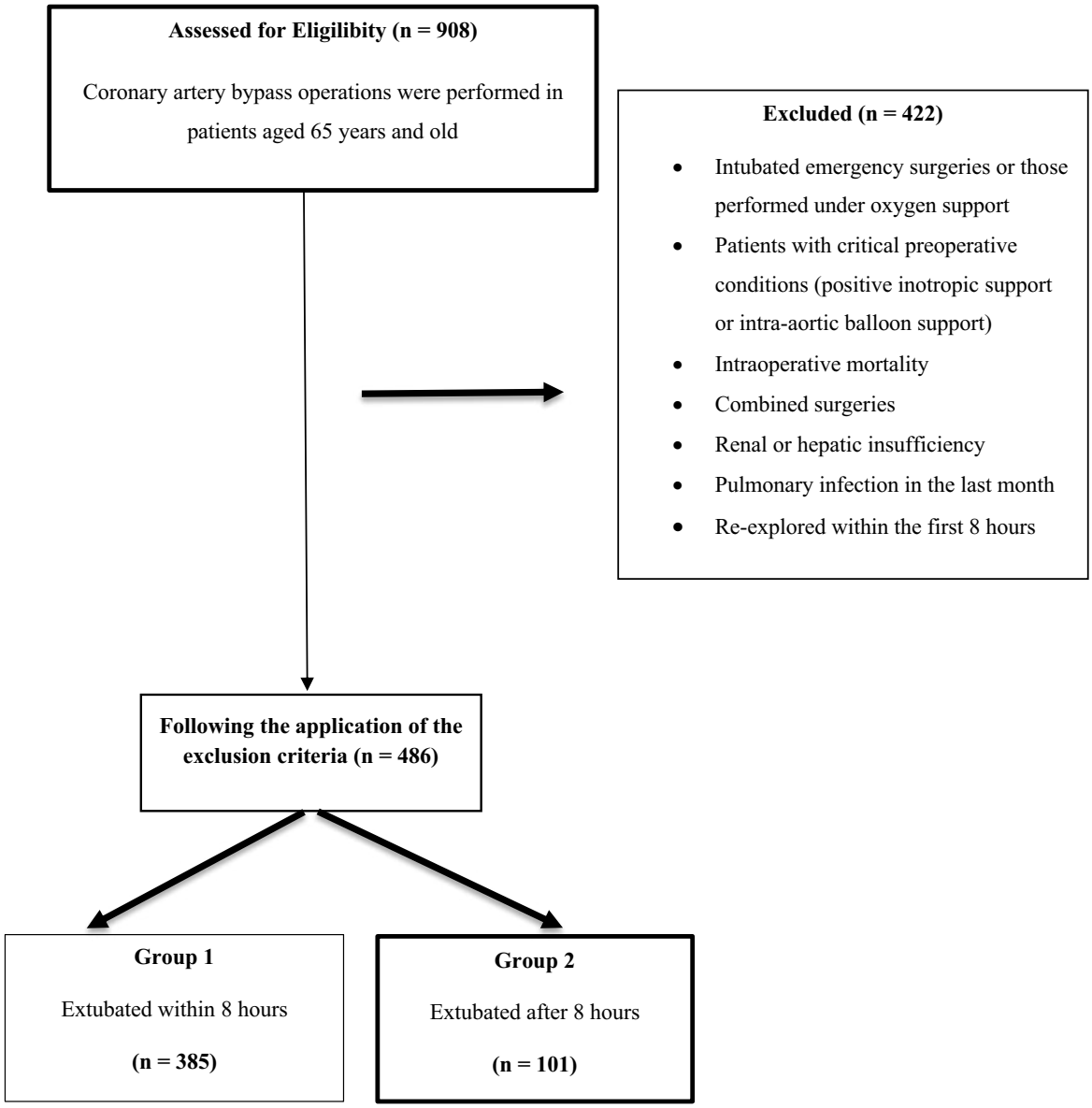

Fig. 1. Flow chart of the study.

of 50% oxygen and 50% air. For intraoperative mechanical ventilation, a Primus® anesthetic machine (Draeger Medical, Germany) was employed. Surgery commenced after an internal jugular vein catheterization. The following parameters were tracked throughout the procedure: temperature, urine output, pulse oximetry, end-tidal carbon dioxide, arterial blood pressure, and electrocardiography. Before the sternotomy, intravenous fentanyl (3-5 g/kg) was added. Before cannulation, heparin (300-400 units/kg) was given to obtain a clotting time of at least 480 seconds. During the entire CPB, midazolam, fentanyl and rocuronium were used to maintain anesthesia. Early extubation was planned in conjunction with avoiding unnecessary sedation and opioid use throughout the operation.

When doing standard CPB, moderate hypothermia (32°C) was used. Aorto-venous two-stage cannulation was used to accomplish CPB after median sternotomy and heparinization. In order to achieve cardiac arrest, the ascending aorta was clamped, and cold antegrade cardioplegia with high potassium was administered (PLEGISOL® | Pfizer). Blood cardioplegia was administered every 15 to 20 minutes to maintain cardiac arrest. CPB was established with a roller pump equipped with a membrane oxygenator and arterial line filter (Maquet, Getinge Group, Germany). The pump's flow

rates were 2-2.4 L/min/m^2. Arterial blood gas was evaluated every 20 to 30 minutes; immediately prior to removing the cross-clamp, 500 milliliters of hot blood cardioplegia were administered.

Postoperative Management

The patients were transferred to the cardiovascular surgery intensive care unit when the surgery was completed and all patients received the usual postoperative care. Patients were evaluated hourly for eligibility for extubation. The provision of hemodynamic stabilization (without the need for high-dose vasoactive inotropic support; urine output > 0.5 mL/kg/hours; without severe arrhythmia) was followed by extubation as soon as it was practicable [12]. Prolonged ventilation was accepted as 8 hours since all operations were performed by avoiding unnecessary use of anesthetic agents in elective and hemodynamically stable patients.

Statistical Analysis

For analysis, IBM SPSS version 21.0 (IBM Corp., Armonk, NY, USA) was utilized. The mean, SD, median (min-max), number, and frequency of the variables were used to express them. To analyze the normality of numerical data, the Kolmogorov-Smirnov and Shapiro-Wilk tests were applied. The Mann-Whitney U test was used to evaluate non-normally distributed variables, whereas the Student's t-test was used to study variables with a normal distribution. Comparing categorical variables was done using the chi-square test. One-Way ANOVA test was used to compare mean mechanical ventilation time according to GPS groups (0, 1, and 2) and subgroup analyzes were performed with Tukey's test (Fig. 2). To examine the predictors of PV, a multivariate logistic regression analysis was used. Statistical significance was defined as a *p* - value of 0.05 or lower.

RESULTS

Prolonged ventilation occurred in 101 (20.7%) patients (Group 2). The median age of the 385 patients included in Group 1 and 101 patients in Group 2 was 68 (66 to 91) and 71 (66 to 88) years, respectively ($p = 0.216$). The two groups were similar in regards to gender, hypertension, smoking, diabetes mellitus, body mass index, history of cerebrovascular events, and left ventricular ejection fraction rates. White blood cells, hemoglobin, platelets, creatinine, urea, and C-reactive protein levels did not significantly differ across the groups. In Group 2, albumin values were significantly lower ($p = 0.014$), whereas the EuroSCORE thereof was significantly higher ($p < 0.001$). Additionally, the GPS classifications between the two groups differed significantly (Table 1). Additionally, in patients with a GPS of 2 mean ventilation time was significantly higher than in patients with a GPS of 0 and 1 (Fig. 2).

The operative features and postoperative complication rates of the patients are presented in Table 2.

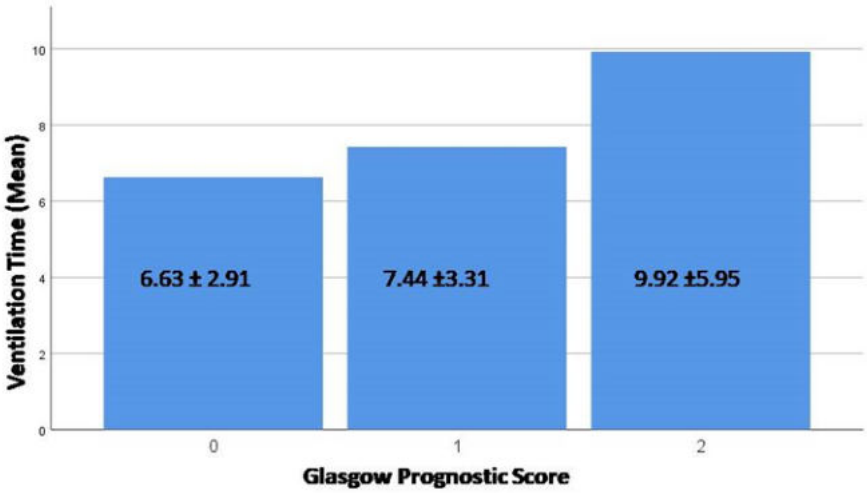

Fig. 2. Mean ventilation times according to Glasgow Prognostic Score (GPS 0 vs GPS1; *P* = 0.096, GPS 0 vs GPS 2; *P* < 0.001, GPS 1 vs GPS 2; *P* < 0.001).

Table 1. Demographic and preoperative features of the patients

Variables	Group 1 (n = 385)	Group 2 (n = 101)	*p* value
Age (years)	68 (66-91)	71 (66-88)	0.216‡
Gender, female, n (%)	107 (27.8)	30 (29.7)	0.704*
Hypertension, n (%)	232 (60.3)	66 (65.3)	0.350*
Diabetes mellitus, n (%)	88 (22.9)	29 (28.7)	0.221*
Current smoker, n (%)	149 (38.7)	44 (43.6)	0.374*
COPD, n (%)	75 (19.5)	26 (25.7)	0.167*
Previous CVA	33 (8.6)	12 (11.9)	0.307*
BMI (kg/m^2)	26.8 (24.3-38.9)	27.3 (24-39.1)	0.325‡
LVEF (%)	50 (25-65)	45 (25-65)	0.116‡
White blood cell (10^3/µL)	6.9 (5.2-11.9)	7.3 (4.8-9.8)	0.447‡
Platelet (10^3/µL)	215 (138-396)	221(128-350)	0.194‡
Hematocrit (%)	38.4 (34.1-50)	39.1 (33.3-47)	0.241‡
Creatinine (mg/dL)	0.96 (0.7-2)	0.98 (0.7-1.96)	0.416‡
Urea (mg/dL)	18 (15-48)	20 (16-42)	0.192‡
C Reactive protein (mg/dL)	8.3 (0.9-28)	8.8 (0.7-26)	0.212‡
Albumin (mg/dL)	38 (30-48)	36 (30-50)	**0.014**‡
EuroSCORE II	3.2 (0.8-6.4)	3.7 (0.8-10.1)	**< 0.001**
GPS = 0/1/2, n	231/115/39	43/30/28	**< 0.001***

Data are shown as median (minimum-maximum). BMI = Body mass index, CVA = Cerebrovascular accident, COPD = Chronic obstructive pulmonary disease, EuroSCORE = European System for Cardiac Operative Risk Evaluation, GPS = Glasgow Prognostic Score, LVEF = Left ventricular ejection fraction

*Chi-square test, ‡Mann Whitney U test

Cross-clamp times, the number of distal anastomoses, packed blood products used, intra-aortic balloon pump need rates and intensive care unit stay-days, were all similar between the two groups. Total perfusion time and postoperative atrial fibrillation rates were statistically significantly higher in Group 2 ($p < 0.001$ and $p = 0.021$, respectively), whereas renal injury, pneumonia, reintubation, and mortality rates were similar between the two groups.

In the univariate analysis, prolonged ventilation development was found to significantly correlate with age > 75 (odds ratio [OR]: 0.796, 95% confidence interval [CI]: 0.554-0.916, $p = 0.021$), ejection fraction < 35% (OR: 1.190, 95% CI: 1.050-1.894, $p = 0.008$), total perfusion time (OR: 1.240, 95% CI: 1.110-1.842, $p < 0.001$), need of inotropic support (OR: 1.370, 95% CI: 1.150-2.248, $p = 0.007$), low albumin value (OR: 0.872, 95% CI: 0.665-0.938, $p = 0.021$), and GPS = 2 (OR: 2.350, 95% CI: 1.696-3.550, $p < 0.001$). In the multivariate analysis, LVEEF < 35% (OR: 1.136, 95% CI: 1.065-1.652, $p = 0.029$), total perfusion time (OR: 1.190, 95% CI: 1.040-1.659, $p = 0.012$), and GPS = 2 (OR: 1.479, 95% CI: 1.130-2.169, $p = 0.004$) were determined as independent predictors for prolonged ventilation (Table 3).

DISCUSSION

Coronary artery bypass graft surgeries, in which CPB systems are mostly used, are performed under general anesthesia. At present, when these operations are planned electively, it is devised that the patients will be extubated as soon as possible during the inten-sive care follow-up. Various studies have been conducted investigating the reasons for longer extubation. In the

Table 2. Operative and postoperative features of the patients

Variables	Group 1 (n = 385)	Group 2 (n = 101)	*p* value
Total perfusion time (min)	83 (57-165)	88 (60-188)	**< 0.001**‡
Cross-clamp time (min)	52 (36-92)	55 (32-88)	0.294‡
Number of distal anastomoses, n (range)	3 (2-6)	3 (2-6)	0.387‡
Packed blood products (units)	4 (2- 6)	4 (2-8)	0.328‡
Inotropic support, n (%)	155 (40.3)	57 (56.4%)	**0.004***
IABP support, n (%)	45 (11.7)	14 (13.9%)	0.552*
Total ICU stay (days)	2 (2- 7)	2 (2- 10)	0.134‡
PoAF, n (%)	90 (23.4)	35 (34.7)	**0.021***
Renal injury, n (%)	97 (25.2)	32 (31.7)	0.189*
Pneumonia, n (%)	39 (10.1)	15 (14.9)	0.179*
Reintubation, n (%)	6 (1.5)	2 (2)	0.767*
Mortality, n (%)	5 (1.3)	2 (1.9)	0.609*

Data are shown as mean ± standard deviation or n (%). IABP = Intra-aortic balloon pump, ICU = Intensive care unit, PoAF = Postoperative atrial fibrillation, Inotropic support = Defined as needs of dopamine, and/or norepinephrine (> 5 mg/kg/min)
*Chi-square test, ‡Mann- Whitney U test

current research, we established that GPS value can be used to predict prolonged ventilation risk in addition to known risk factors.

Albumin is an important protein that makes up more than half of body serum proteins. In addition to its anti-inflammatory and antioxidant properties, it also has physiological properties such as anticoagulant and inhibition of platelet aggregation. In addition to all these, it also plays an important role in transmembrane fluid passages in the body [13]. Various studies have shown that cardiovascular disease development and progression are influenced by decreased albumin levels. While hypoalbuminemia has been reported at a rate of 25% in patients with chronic heart failure,

Table 3. Logistic regression analysis to identify factors affecting development of prolonged ventilation

Variables	Univariate analysis			Multivariate analysis		
	p value	Exp(B) Odds Ratio	95% CI Lower-Upper	*p value*	Exp(B) Odds Ratio	95% CI Lower-Upper
Age > 75	**0.021**	0.796	0.554-0.916	0.240	0.884	0.791-1.117
LVEF < 35%	**0.008**	1.190	1.050-1.894	**0.029**	1.136	1.065-1.652
COPD	0.144	1.214	0.849-1.453	--	--	--
C-reactive protein	0.192	0.940	0.781-1.438	--	--	--
Total perfusion time	**< 0.001**	1.240	1.110-1.842	**0.012**	1.190	1.040-1.659
Inotropic support	**0.007**	1.370	1.150-2.248	0.124	0.985	0.785-1.132
Albumin	**0.021**	0.872	0.665-0.938	--	--	--
GPS = 2	**< 0.001**	2.350	1.696-3.550	**0.004**	1.479	1.130-2.169

LVEF = Left ventricular ejection fraction, COPD = Chronic obstructive pulmonary disease, GPS = Glasgow prognostic score
The goodness of fit of the multivariate model was confirmed by a *p*-value of 0.784 in the Hosmer-Lemeshow test.

this rate has been reported up to 90% in the elderly and patients with acute heart failure [14].

The importance of albumin was investigated in a prospective study of 734 clinically stable patients with known coronary artery disease. In this study, patients were followed for 18 months and low albumin was demonstrated as an independent predictor of all-cause mortality and cardiovascular mortality [15]. In a prospective study including 588 patients, low albumin levels were found to be a reliable indicator of long-term death after CABG procedures [16]. Because of these properties, albumin has been included in various evaluation parameters used as prognostic value (the Essential Frailty Toolset, the Prognostic nutritional index, GPS, etc). In one study, the relationship between a low prognostic nutritional index and postoperative atrial fibrillation was revealed [17]. In another study conducted by Solomon *et al*. [18], patients aged 60 years and older who underwent CABG were included. Low albumin levels have been linked to all-cause postoperative mortality in this research of 500 patients with a mean age of 71.4 ± 6.4 years.

An essential acute phase reactant is the C-reactive protein. It belongs to the pentraxin protein family and activates classical and alternative complement pathways. It also induces cytokine release by activating leukocyte. In addition, CRP deposits were found in atherosclerotic foci taken from human arteries in various histological studies [19]. Studies have investigated the prognostic importance of preoperative CRP values after CABG operations. In one of these, high CRP levels before surgery have been linked to myocardial injury and low cardiac output after CABG operations [20]. In another study by Nam *et al*. [21], the prognostic role of preoperative CRP value was investigated in patients who underwent off-pump CABG operation. The authors revealed a significant relationship between postoperative mortality and high CRP values.

The GPS value is a parameter created by considering CRP and albumin values. Studies examining the connection between GPS and various cancers have been conducted in the literature, and the importance of GPS value has been demonstrated [22, 23]. Recent studies have also investigated the relationship between cardiovascular diseases and GPS. In a study by Xu *et al*. [24], the relationship between the development of major adverse events and GPS in patients with acute coronary syndrome was investigated. The authors found that the risk of developing major adverse events increased more than five times in patients with a GPS value of 2, compared to patients with a GPS value of 0 [24]. Cho *et al*. [25], on the other hand, investigated the prognostic value of GPS value in their study, which included 443 patients with stable heart failure. The authors demonstrated in this study that there is a significant relationship between high GPS values and the development of adverse events [25]. In the study conducted by Altay *et al*. [26], the relative importance of the GPS value in predicting the prognosis was investigated in some 1 004 patients requiring cardiovascular intensive care. As a result of the multivariate analysis, it was concluded that in-hospital mortality was seven times higher in patients with a GPS value of 2 compared to patients with a GPS value of 0 [26]. In a recent study, the importance of GPS value was investigated in patients who underwent transcatheter aortic valve implantation. The endpoints in this study were in-hospital mortality, cardiac rehospitalization and one-year death. At the end of the study, GPS value was shown as an independent predictor of forecasting endpoints [11].

In a study by Hessels *et al*. [27], factors affecting prolonged ventilation time after cardiac surgery were investigated. The median age of the patient group in this study was 67 years and 11% of the patients had more than 24 hours of ventilation. In this study, low ejection fraction, combined surgery, urgency of surgery, use of IABP, increased blood product use and prolonged CPB times, were found to be related to prolonged ventilation [27]. However, in this study, explanatory information about the anesthesia management of the patients was not provided. Our study, unlike the latter, was planned for patients aged 65 and over who underwent elective isolated CABG surgery. Our anesthesia management was performed in such a way as to allow the earliest extubation of all patients. For this reason, the prolonged ventilation duration was determined as eight hours. In our study, similar to Hessels *et al*., we found low LVEF, increased blood product use and long CPB times to be associated with prolonged ventilation times. In a study by Gumus *et al*. [28], the risk factors of prolonged ventilation after CABG operations were investigated

and with similar to ours, a significant relationship was found between long CPB times and prolonged ventilation.

Limitations

Although we uncovered valuable information in our study to contribute to the literature, there are some limitations. The first is that ours was a single-center retrospective study, therefore the number of patients was also limited. In our study, LVEF < 35% and the need for inotropic support were significantly correlated with prolonged ventilation. Although not statistically significant, the rates of postoperative atrial fibrillation and renal injury were also higher in patients with prolonged ventilation. Increased use of inotropic agents may also have increased these complication rates.

CONCLUSION

It is crucial to perform extubation as early as possible after CABG operations in patients with stable preoperative hemodynamics under elective conditions. In this study, we revealed that the GPS value calculated preoperatively in elderly patients is a parameter that indicates the prolonged ventilation. With the GPS score evaluation, patient groups at risk for prolonged ventilation may be identified and necessary precautions may be undertaken.

Institutional Review Board Statement

The study was approved by Bursa Yuksek Ihtisas Training and Research Hospital's clinical research ethics committee (2011-KAEK-25 2022/10- 03).

Informed Consent Statement

Written informed consent was obtained from the patients before their interventions.

Authors' Contribution

Study Conception: OG, ME; Study Design: OG; Supervision: OG, ME, ŞY; Funding: OG, ME; Materials: OG, ME, IIK; Data Collection and/or Processing: OG, ME; Statistical Analysis and/or Data Interpretation: OG, IIK; Literature Review: OG, ME, IIK, ŞY; Manuscript Preparation: OG, ME and Critical Review: OG, ME, IIK, ŞY.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

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