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Preoperative Vitamin D Level Predicts Operative Mortality After Cardiac Surgery

Atike Tekeli Kunt[1], Naim Boran Tümer[2], Kanat Özışık[2], Serdar Günaydın[2]

[1]Kırıkkale University Faculty of Medicine, Department of Cardiovascular Surgery, Kırıkkale, Turkey
[2]University of Health Sciences Turkey, Ankara City Hospital, Clinic of Cardiovascular Surgery Ankara, Turkey

Abstract

Objectives: The present study aimed to analyze the prognostic value of preoperative serum vitamin D level in patients who underwent coronary artery bypass graft (CABG) surgery.

Materials and Methods: The data of 360 adult patients who underwent isolated CABG surgery were retrospectively reviewed. We reached the data of preoperative serum vitamin D [25-hydroxyvitamin D (25-OHD)] values of 305 patients. The patient population was divided into two groups based on preoperative serum 25-OHD levels with a normal range of 25-75 nmol/L (group I: patients with preoperative serum 25-OHD level <25 nmol/L and group II: patients with preoperative serum 25-OHD level ≥25 nmol/L). The effect of preoperative 25-OHD level on operative mortality (mortality which occurred during the first 30 days after the operation) was determined using regression analysis and the results were expressed as Odds ratio (OR) with a 95% confidence interval (CI). A p value <0.05 was considered statistically significant.

Results: In the present study, operative mortality was 3.93% (n=12). One hundred and fifty seven patients (51.5%) had serum 25-OHD levels <25 nmol/L. The mean serum 25-OHD levels were significantly lower in females than in males (p<0.001). On logistic regression analysis, preoperative serum 25-OHD level was found to be independently associated with operative mortality (OR: 0.201, 95% CI: 0.043- 0.935; p=0.041).

Conclusion: The presence of vitamin D deficiency seems to be an independent predictor of operative mortality after cardiac surgery in this retrospective study; however, prospective randomized trials are warranted to clarify the effect of preoperative vitamin D supplementation on postoperative outcomes in cardiac surgical patients.

Keywords: Vitamin D, cardiac surgery, operative mortality

Address for Correspondence: Atike Tekeli Kunt, Kırıkkale University Faculty of Medicine, Department of Cardiovascular Surgery, Kırıkkale, Turkey
e-mail: atikemd@gmail.com **ORCID:** orcid.org/0000-0001-9764-7393
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Introduction

Robert Goetz was the first to perform coronary artery bypass grafting (CABG) surgery in 1960, and after that CABG became the most commonly performed cardiac surgery procedure worldwide[1,2]. Despite technological advances and advancements of surgical experience and perioperative care, the short term (in-hospital and/or 30-day) mortality of CABG varies from 1% to 5%[3]. To predict the operative mortality which occur during the first 30 days after CABG, several risk scoring systems and additional tools as biomarkers have been developed[4,5]. The most commonly used and well-known biomarkers are troponins, brain natriuretic peptide and N-terminal fragment of brain natriuretic peptide[6,7].

Vitamin D is a steroid hormone and has a role in bone metabolism. It is produced on the skin by the effect of sunlight. It is also important for immunity, cardiovascular, and central nervous systems[8]. It is known to play a role in the metabolism of insulin and the development of obesity[9]. Vitamin D deficiency is a global health problem and many adults and also infants have low vitamin D levels worldwide[10]. Vitamin D has protective effects on atherosclerosis by increasing nitric oxide levels and decreasing oxidative stress in endothelium and also by inhibiting the proliferation of smooth muscle cells in vessels; thus, vitamin D deficiency is suggested to be associated with increased risks of coronary artery disease[11]. In the present study, we analyzed the association of preoperative vitamin D levels with operative mortality in patients who underwent CABG surgery.

Materials and Methods

Patients

We retrospectively reviewed the data of 360 adult patients who underwent isolated CABG surgery from January 2016 to January 2018. We reached the data of preoperative serum vitamin D [25-hydroxyvitamin D (25-OHD)] values of 305 patients. All patients previously had granted permission for the use of their medical records for research purposes and institutional review board approved the study (no: E-19-048, date: 3.10.2019, Ankara City Hospital). For the present study, the patient population was divided into two groups based on preoperative serum 25-OHD levels with a normal range of 25-75 nmol/L (group I: patients with preoperative serum 25-OHD level <25 nmol/L and group II: patients with preoperative serum 25-OHD level ≥25 nmol/L). The primary outcome was the operative mortality. Operative mortality was defined as mortality which occurred during the first 30 days after the operation**.** Patients with recent myocardial infarction, emergent surgery, and patients undergoing operations other than CABG or in conjunction with CABG were excluded from the study.

All operations were performed in a standardized approach and by the same surgical team. Terumo roller pump (Terumo Advanced Perfusion System 1, USA) and membrane oxygenators (Inspire 8, LivaNova Sorin Group, Italy) were used with mild to moderate (28-32 °C) hypothermia and pulsatile flow of 2.2-2.4 L/m^2. Myocardial protection was achieved with tepid antegrade blood cardioplegia. Patients were followed in the intensive care unit (ICU), in accordance with the protocols of our institution.

Statistical Analysis

All statistics were performed using SPSS version 18.0 for Windows (IBM Corporation, New York, USA). Continuous variables were expressed as mean ± standard deviation and were compared by unpaired Student's t-test or chi-square test. The effect of preoperative serum 25-OHD level on operative mortality after CABG was determined using logistic regression analysis, and the results were expressed as Odds ratio (OR) with a 95% confidence interval (CI). A p value <0.05 was considered statistically significant.

Results

In this study, 51.5% of patients had preoperative serum 25-OHD levels <25 nmol/L. Preoperative patient characteristics and intraoperative data did not show statistical significance between the two groups other

than gender, vitamin D levels, and Euroscore II (Table 1). The preoperative mean serum 25-OHD was 19.1±4.4 nmol/L in group I and 48.2±16.4 nmol/L in group II (p<0.001). Preoperative mean serum 25-OHD levels were significantly lower in females than in males (31.0±18.4 nmol/L, 35.6±18.8 nmol/L, respectively p=0.035). On logistic regression analysis, the presence of lower serum 25-OHD levels was shown to be associated with an increased incidence of operative mortality (OR: 0.201, 95% CI: 0.043-0.935; p=0.041). Logistic regression analysis also revealed that Euroscore II was the other independent risk factor for operative mortality after isolated CABG in this study (OR: 1.270, 95% CI: 1.034-1.559, p=0.023).

The postoperative data of the patients are shown in Table 2. Prolonged ventilatory support was necessary in 3.8% of patients. Postoperative acute kidney injury was observed in 17% of patients. Kidney injury was interpreted according to RIFLE classification[12]; RIFLE (R: risk, I: injury, F: failure, L: loss, and E: end-stage kidney disease). When results were compared according to the RIFLE classification, 36 patients were in group I and 16 patients were in group II (p=0.004). Operative mortality was 3.93%. Nine patients died due to low cardiac output and multiorgan failure during the hospital stay, one patient died due to pulmonary embolism on the 15th postoperative day, one patient due to mediastinitis on the 23rd postoperative day, and one patient died due to cerebrovascular accident on the 18th postoperative day.

Table 1. Baseline and perioperative characteristics of patients

Clinical characteristics	Group I* (n=157)	Group II** (n=148)	p
Age, years	69.8±7.1	68.2±8.0	0.359
Female (n)	95	62	**0.001‡**
Body mass index, kg/m²	27.2±4.7	28.1±4.9	0.237
Hypertension (n)	91	87	0.488
Diabetes mellitus (n)	64	74	0.066
Hyperlipidemia (n)	90	78	0.243
Serum 25-OHD (nmol/L)	19.1±4.4	48.2±16.4	**<0.001‡**
CPB time (min)	109.6±41.3	102.7±39.5	0.063
Cross-clamp time (min)	62.1 ±22.6	58.6±24.7	0.168
LV function (%)	52.4±10.7	54.4±9.4	0.052
Serum creatinine (mg/dL)	0.95±0.2	0.92±0.2	0.219
Creatinine clearance (mL/min)	84.1±35.9	90.1±35.2	0.156
Euroscore II (%)	3.9±2.6	2.9±2.1	**0.009‡**

CPB: Cardiopulmonary bypass, LV: Left ventricle, n: Number
**Group I: patients with preoperative serum 25-OHD levels <25nmol/L, **Group II: patients with preoperative serum 25-OHD levels ≥25 nmol/L. ‡p<0.05, statistically significant*

Discussion

The aim of the present study was to determine whether preoperative serum 25-OHD levels were associated with operative mortality after CABG. Our retrospective study illustrated that lower preoperative serum level of 25-OHD was associated with operative mortality. Our results showed that 51.5% of patients had preoperative serum 25-OHD levels <25 nmol/L. It is known that vitamin D deficiency rate is increasing worldwide and approximately 30% of people in all age groups have deficiency or insufficiency[13]. Vitamin D deficiency is common among older and critically ill patients. As we analyzed the cardiac surgical patients who were old and critically ill in nature, our results were similar with literature in this regard[14].

Vitamin D deficiency is reported to be associated with increased morbidity and even mortality in critically ill patients[15-17]. Although the exact mechanism to elucidate this association is not well understood, higher incidence of postoperative inflammatory processes in vitamin D deficiency may be one of the explanations[18]. Cardiac

Table 2. Postoperative data of the patients

	Group I* (n=157)	Group II** (n=148)	p
Mean ICU time (h)	55.3±25.9	49.3±22.2	0.031‡
Mean ventilatory support time (h)	9.2±11.4	7.2±2.2	0.038‡
IABP support (n)	12	3	0.032‡
In-hospital stay time (d)	6.8±2.5	6.2±1.6	0.013‡
Operative mortality (n)	12	2	0.036‡

ICU: Intensive care unit, h: hours, IABP: Intra-aortic balloon pump, d: Days, n: Number
**Group I: patients with preoperative serum 25-OHD levels <25nmol/L, **Group II: patients with preoperative serum 25-OHD levels ≥25 nmol/L. ‡p<0.05, statistically significant*

surgical patients are at risk of surgery-related inflammation. Cardiopulmonary bypass (CPB) results in an acute systemic inflammatory response syndrome and this is suggested to result in increased morbidity, development of organ dysfunctions, and mortality[19]. The inflammatory cascade is activated during CPB and proinflammatory cytokines as interleukin-6 (IL-6) and IL-8 are released, which results in immune system dysfunction[20,21]. The anti-inflammatory effects of vitamin D are documented and preoperative lower levels of vitamin D are found to be associated with postoperative organ dysfunction and mortality[14,22]. Additionally, experimental studies have indicated that due to the attenuation of vascular inflammation in vitamin D deficiency, cardiovascular risk increases[23]. Low levels of vitamin D, which result in decreased anti-inflammatory capacity after cardiac surgery, could contribute to poor outcomes and increased operative mortality in the present study.

Our results revealed an increased ICU stay time and hospital stay times in patients with vitamin D deficiency, which is compatible with the studies in the literature[19,23]. It was reported by Abou Zahr et al.[24] that vitamin D levels were decreased immediately after CPB and increased after 24 hours. The explanation of the reduction was attributed to acute fluid shifts during CPB and the rise was attributed to renal recovery with improved perfusion after CPB. Recently, there are studies dealing with the role of vitamin D in postoperative outcomes[25]. It has been suggested that preoperative vitamin D deficiency is associated with acute kidney injury, acute respiratory distress syndrome, neurologic dysfunctions, nosocomial infections, liver dysfunction, and cardiogenic shock after cardiac surgery[22]. Acute kidney injury was reported to be higher in group I in our study. Vitamin D supplementation is another issue that needs to be clarified as there is no consensus regarding whether it is necessary to supply vitamin D preoperatively or not, when to supply or in which dose it should be supplied. It is suggested that vitamin D supplementation may play a protective role against paroxysmal atrial fibrillation after cardiac surgery[26]. It is also reported that the optimization of vitamin D status in both critically ill adults and congenital heart disease patients could attenuate inflammation and nosocomial infection and improve cardiac function[27].

Another finding in our study was the gender difference between the two groups. Vitamin D deficiency was more common among females in the present study. Quraishi et al.[28] also reported vitamin D deficiency in females in their study; however, Ford et al.[29] reported a higher prevalence of vitamin D deficiency among men and stated that the amount of body fat and/or its distribution could explain this gender difference.

The other independent risk factor for operative mortality in our study was found to be increased Euroscore II. Additive Euroscore II has been used worldwide in the clinical practice since 1999 and Euroscore II since 2012 for mortality prediction after cardiac surgery. Euroscore II, which is also used in our study, is suggested to be a good predictor of mortality in low risk cardiac surgical patients: however, it may underestimate mortality especially in high risk population[30].

Study Limitations

There are some limitations of the present study. First, the study design was retrospective. Second, in the study, the sample size was relatively small and was limited to CABG patients and finally, we did not perform a propensity score matching to analyze the effect of Euroscore II or vitamin D deficiency on mortality.

Conclusion

In summary, the incidence of Vitamin D deficiency was 51.5% and the operative mortality was 3.93% in the present study. Vitamin D deficiency resulted in poor postoperative outcomes and increased operative mortality after CABG. Prospective randomized studies that are designed to analyze the effect of vitamin D deficiency and its supplementation before surgery on postoperative outcomes are warranted.

Ethics

Ethics Committee Approval: Institutional Review Board of Ankara City Hospital approved the study (no: E-19-048, date: 3.10.2019).

Informed Consent: All patients previously had granted permission for the use of their medical records for research purposes.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: A.T.K., N.B.T., K.Ö., S.G., Concept: A.T.K., N.B.T., K.Ö., S.G., Design: A.T.K., N.B.T., K.Ö., S.G., Data Collection or Processing: A.T.K., N.B.T., K.Ö., S.G., Analysis or Interpretation: A.T.K., N.B.T., K.Ö., S.G., Literature Search: A.T.K., N.B.T., K.Ö., S.G., Writing: A.T.K., N.B.T., K.Ö., S.G.

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