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# Influence of Postoperative Anemia on Functional Capacity Recovery in Patients Undergoing Coronary Artery Bypass Grafting

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## Abstract

**Background:** Postoperative anemia (PPA) is a prevalent comorbidity after cardiac surgery. This study investigated the association between functional capacity (FC) recovery and postoperative anemia (PPA).

**Methods:** We retrospectively analyzed 120 patients who received coronary artery bypass grafting. The lowest hemoglobin (Hb) data during hospitalization was collected. We divided the patients into two groups on the basis of hemoglobin (Hb) median value, defined as severe and mild anemia group. Peak oxygen consumption based on the results of a cardiopulmonary exercise test (CPXT) after discharge was used as the primary index of functional capacity (FC). For data analysis, T-test and Chi-Square test were used to compare group differences. Logistic regression was performed to compare the functional capacity recovery between groups. Linear regression was used to identify the effects of post-operation infusion in advanced. Statistical significance was a P value of 0.05.

**Results:** Most of the patients were men (73.3%), and the mean age was 64.3 ± 10.5 years. All the patients had postoperative anemia (PPA) during hospitalization. The median value of lowest hemoglobin (Hb) during hospitalization was 8.8 g/dL. Patients in mild anemia group had 3.2-fold higher odds of functional capacity (FC) recovery to 3.5 METs when they discharge from hospital. Even post-operation infusion was given the severe anemia patients would still had worse functional capacity (FC) recovery.

**Conclusions:** Powered by Editorial Manager® and ProduXion Manager® from Aries Systems Corporation Postoperative anemia (PPA) is a notable problem in CABG patients. Patients who have hemoglobin (Hb) levels <8.8 g/dL during hospitalization may not attain the expectedfunctional capacity (FC) after discharge.

**Keywords:** Anemia; Hemoglobin; Hospitalization; Mortality

## Introduction

Postoperative anemia (PPA) is a common complication of cardiac surgery. The prevalence of postoperative anemia has increased because blood transfusion is recommended only in patients with extremely severe anemia, those with hemoglobin (Hb) levels <6 g/dL, or in those with hemodynamic instability [1]. PPA is generally considered an acute status that may recover spontaneously. However, a previous study reported that nearly 30% of patients had sustained anemia after 1 month [2].

In our preliminary study, we reviewed patients who received coronary artery bypass grafting (CABG) and determined a prevalence rate of up to 98.9%, which was higher than that reported for other surgeries. The lowest Hb value appeared on the fourth to fifth day after operation and was 9.0 ± 1.4 g/dL on average. The recovery trend was similar to those of previous reports; otherwise, the prevalence rate was higher.

Anemia has been identified as a risk factor for mortality and increases the mortality rate by 1.4–3.4-fold, particularly in patients with Hb levels <11 g/dL. Moreover, during a 30–40-month follow-up, anemia was strongly associated with an increased mortality rate and the risk of heart failure in patients with sustained anemia 1 month after discharge [2]. Meanwhile, the association between physical capacity and anemia is evident. A positive association between anemia severity and peak oxygen consumption ($VO_2$ peak) was observed after adjustment for age, body mass index, and activity status [3]. In Ranucci's study [4], they found that Hb value might influent functional capacity. They recruited cardiac patients who at the rehabilitation onset, patients with Hb levels <10 g/dL performed worse on the six-minutes walking test (6 MWT) than those with Hb levels >10 g/dL. However, the study did not exclude patients with anemia before cardiac surgery. Patel [5] used another measurement, short form-36 questionnaire (SF-36), to identify the physical function and explained the outcome according to the patients' baseline characteristics rather than anemia. Except the results were inconsistence, no related studies have investigated the post-cardiac surgery population who may face the problem more seriously.

We examined whether PPA severity during hospitalization would influence the functional capacity recovery at discharge in patients after CABG surgery.

## Materials and Methods

### Population

In this retrospective cohort study, we included patients who had undergone traditional CABG between November 2013 and November 2014. The inclusion criteria were an age > 18 years and normal Hb levels (13 and 12 g/dL for men and women, respectively) before CABG. We excluded patients who withdrew from inpatient cardiac rehabilitation

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or did not undergo cardiopulmonary exercise testing (CPXT) after discharge.

### Measurements

The independent variable: anemia and hemoglobin value.

All of the Hb value was derived from the results of blood tests. Serial Hb value was collected every day in the intensive care unit and twice per week in the ward after operation. If the lowest value of Hb during hospitalization lower than normal value (According to the definition of WHO, the Hb<13 in male or Hb<11 in female), we recognized the subject have PPA. Among these PPA patients, we divided them into two groups on the basis of the median value of the lowest Hb data (severe vs mild anemia group).

### Other associated variables

We obtained baseline information from medical charts review. Personal characteristics of sex, age, body height and weight, body mass index, cardiac risk factors, and education levels were assessed. Clinical factors such as left ventricular ejection fraction (LVEF), lung function (forced vital capacity [FVC], forced expiratory volume in 1 second [FEV1], and FEV1/FVC), blood serum chemistry, and hematological values (white bloods cells, platelets, and blood urea nitrogen) were examined. LV function was classified as preserved, mild, moderate and severe dysfunction based on the LVEF (>50%, 40-49%, 30-39%, and <30% respectively). Therapeutic factors such as surgery type, surgery duration, blood transfusion during or after surgery, and medications were also assessed.

### Cardiac pulmonary exercise testing

CPXT was performed in one month after discharge. The primary index of functional capacity was $VO_2$ peak (mL/kg/min), which was converted to the metabolic equivalent (MET). On the basis of the New York Heart Association functional classification, we used 3.5 METs to categorize patients reach acceptable functional capacities. CPXT, administered according to the recommendations of the 2002 American College of Cardiology/American Heart Association guidelines, is a symptom-limited graded exercise test, in which the treadmill was the main exercise mode, and a modified Bruce protocol was used. Exercise capacity was measured using a Vmax 29c Cardiopulmonary Stress System (SensorMedics Corporation, USA).

## Data Analysis

Analyses were performed using SPSS Version 17.0 (SPSS Inc, Chicago, IL, USA). We used $X^2$ (for binary variables) and *t* tests (for continuous variables) to assess the significance of any difference in the baseline variables between groups. Logistic regression (LG) was performed to analyze the different severity of PPA on functional capacity recovery. To eliminate the effects of confounding factors, we also put covariates which were significantly different between groups in univariate analysis and those may affect functional recovery into LG analysis. A "P" value of 0.05 was considered statistically significant for all analyses.

## Results

We retrospectively analyzed 120 patients. Most of them were men (73.3%), and the mean age was 64.3 ± 10.5 years. The baseline demographics, clinical characteristics, and exercise performance after discharge are listed (Table 1). All patients had PPA during hospitalization. The median value of the lowest Hb during hospitalization was 8.8 g/dL, and the numbers of patients in mild and severe anemia group were 57 and 63, respectively.

Most of the baseline characteristics were no significant difference between groups (Table 1), except the post-operation infusion. The covariates put into regression model were post-operation infusion and known confounders of functional capacity recover: age, gender, LVEF and whether patients receive hemodialysis. After adjusting possible confounding factors, patients with mild anemia after surgery had a 3.2-fold higher probability of recovery to 3.5 METs after discharge (P = 0.03) compared to severe anemia group (Table 2).

## Discussion

Anemia has been reported in several studies, in which increasing event rates and prolonged hospital stays were the outcome variables in heart failure (HF) and post-cardiac-surgery patients. In a review, Kulier [6] confirmed that low preoperative Hb levels were repeatedly identified as a major predictor of adverse postoperative events and have therefore been included in several preoperative risk stratification models. In addition, anemia may be both a contributor to and a result of HF as a chronic disease state. As McCullough suggested, anemia is associated with increased rates of mortality, hospitalization, and HF exacerbation [7]. However, information regarding functional capacity recovery and exercise tolerance after cardiac surgery is lacking. Anemia has been associated with a decline in physical performance [8-10], including functional decline in activities of daily living. Functional capacity has been proved as a predictor of cardiovascular risk among healthy adults [11-13], and the association between functional capacity

| | Total (n=120) | Severe anemia (n=63) | Mild anemia (n=57) |
|---|---|---|---|
| Age, years | 64.3 ± 10.5 | 64.9 ± 10.7 | 63.7 ± 10.2 |
| Male/Female | 88(73.3)/32(26.7) | 46/15 | 42/17 |
| BMI[a], kg/M$^2$ | 26.4 ± 3.6 | 26.9 ± 3.7 | 25.9 ± 3.4 |
| HTN[b] | 96 (80.0) | 53 | 43 |
| Abnormal lipid profile | 70 (58.3) | 32 | 38 |
| Type 2 DM[c] | 62 (51.7) | 35 | 27 |
| Sedentary lifestyle | 46 (38.3) | | |
| Pre-OP[d] NYHA level | | | |
| Level I | 12 (10.0) | 6 | 6 |
| Level II | 66 (55.0) | 32 | 34 |
| Level III | 34 (28.3) | 17 | 17 |
| Level IV | 7 (5.8) | 5 | 2 |
| Pre-OP LV[e] function | | | |
| Preserved | 75 (62.5) | 36 | 39 |
| Mild dysfunction | 11 (9.2) | 4 | 7 |
| Moderate dysfunction | 11 (9.2) | 6 | 5 |
| Severe dysfunction | 17 (14.2) | 11 | 6 |
| N/A | 6 (5) | 4 | 2 |
| Comorbidity | | | |
| Myocardial infarction | 7 (5.8) | 5 | 2 |
| Chronic liver disease | 2 (1.7) | 2 | 0 |
| Kidney disease | 10 (8.3) | 7 | 3 |
| Hemodialysis | 9 | 7 | 2 |

Data are presented as mean ± SD or No. of patients (%). Baseline demographic and clinical characteristics were no significant differences between groups in X2 (for binary variables) and t tests (for continuous variables) analysis. [a]body mass index; [b]hypertension; [c]diabetes mellitus; [d]pre-operation; [e]left ventricular.

**Table 1:** Baseline demographic and clinical characteristics.

| | Total (n=120) | Severe anemia (n=63) | Mild anemia (n=57) |
|---|---|---|---|
| Age, years | 64.3 ± 10.5 | 64.9 ± 10.7 | 63.7 ± 10.2 |
| Male/Female | 88(73.3)/32(26.7) | 46/15 | 42/17 |
| BMI[a], kg/M$^2$ | 26.4 ± 3.6 | 26.9 ± 3.7 | 25.9 ± 3.4 |
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| Severe dysfunction | 17 (14.2) | 11 | 6 |
| N/A | 6 (5) | 4 | 2 |
| Comorbidity | | | |
| Myocardial infarction | 7 (5.8) | 5 | 2 |
| Chronic liver disease | 2 (1.7) | 2 | 0 |
| Kidney disease | 10 (8.3) | 7 | 3 |
| Hemodialysis | 9 | 7 | 2 |

Data are presented as mean ± SD or No. of patients (%). Baseline Functional capacity and exercise responses were no significant differences between groups in X2 (for binary variables) and t tests (for continuous variables) analysis. [a]body mass index; [b]hypertension; [c]diabetes mellitus; [d]pre-operation; [e]left ventricular.

**Table 2:** Functional capacity and exercise responses.

| | n | Odds ratio (95% CI[a]) | *p* value |
|---|---|---|---|
| Severe anemia | 63 | ref[c] | 0.03 |
| Mild anemia | 57 | 3.2 (1.1-9.5) | |
| Hemodialysis | | | 0.95 |
| Yes | 9 | ref | |
| No | 105 | 1.1 (0.2-6.7) | |
| Postop infusion | | | 0.52 |
| Yes | 67 | | |
| No | 47 | 1.4 (0.5-4.4) | |
| LV[b] function | | | 0.25 |
| Severe dysfunction | 17 | ref | |
| Mod dysfunction | 11 | 0.6 (0.1-4.0) | |
| Mild dysfunction | 11 | 1.3 (0.2-11.3) | |
| Preserved | 75 | 2.5 (0.7-9.7) | |
| Gender | | | 0 |
| Male | 84 | ref | |
| Female | 30 | 0.1 (0.0-0.4) | |
| Age | 120 | 0.9 | 0 |

[a]confidence interval; [b]left ventricle ; [c]reference

**Table 3:** Results of multivariate logistic regression.

and all-cause mortality is noteworthy. Podrid et al. [14] reported increased mortality in patients achieving <6 METs, whereas McNeer et al. [15] and Weiner et al. [16] have determined that 5 and 2 METs, respectively, predicted coronary artery disease (Table 3).

The current study focused on functional capacity recovery in patients with PPA, which is an increasingly prevalent surgical outcome. According to the recommendations of the American College of Sports Medicine guidelines, functional capacity recovery by the end of the hospital stay should be 3–4 METs in post-CABG patients. Our results demonstrate that PPA is a major problem in post-CABG patients. Patients may not attain the expected functional capacity (3.5 METs) after discharge if the Hb level is <8.8 g/dL during hospitalization.

The safety of a restrictive transfusion policy in cardiac surgeries has been addressed in several randomized controlled trials [17-19], in which the outcome variables were morbidity and mortality. Our results demonstrated that the patients in severe anemia group had higher possibility to receive post-operation infusion, though the treatment may not give them extra benefits considering functional capacity outcomes. We believe that blood transfusion may be necessary only in extreme severe anemia patients. Aerobic exercise training after CABG results in an early favorable change in treadmill performance and fibrinogen concentrations [20]. Ranucci [4] reported that the functional gap was completely recovered during a normal rehabilitation period, concluding that a strategy of avoiding impaired exercise tolerance after discharge in postoperative anemia (Hb = 8–10 g/dL) patients. Although the aforementioned studies have not excluded patients with a history of anemia before surgery, it is unclear whether the rehabilitation program is beneficial to patients with PPA after cardiac surgery. Additional studies are warranted to further clarify this association.

The safety of a restrictive transfusion policy in cardiac surgeries has been addressed in several randomized controlled trials [17-19], in which the outcome variables were morbidity and mortality.

## Limitations

Several limitations must be considered. We retrospectively reviewed a selected population of CABG patients (only traditional CABG). The Hb levels were assessed at certain time points and not every day; therefore, we cannot comment on the importance of the change in Hb levels over time. Anemia treatment using transfusion or other medications during the study was not documented or included in the analysis, although these patients were not routinely treated using transfusion, or iron or EPO therapy. Transfusion policy may differ between physicians. Most patients received physical activity training after surgery, which may have contributed to functional capacity recovery. A longer-term study design and serial Hb data will assist health care providers in managing PPA and functional capacity recovery.

## Conclusions

PPA is a major problem in post-CABG patients. Patients may not attain the expected functional capacity (3.5 METs) after discharge if the Hb level is <8.8 g/dL during hospitalization.

## Disclosure Statement

The study received a research grant from Cheng Hsin General Hospital.

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