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## Clinical and Socio-demographic Predictors of Postoperative Vital Exhaustion in Patients after Cardiac Surgery

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### Abstract

**Background**—Vital exhaustion, a psychological state characterized by extreme fatigue, is an independent predictor of future cardiac events. However, the attributes of vital exhaustion following coronary artery bypass (CABG) surgery are poorly understood.

**Objective**—The study objective was to assess correlates of vital exhaustion following CABG surgery.

**Methods**—In a descriptive, exploratory study, 42 patients who had CABG surgery were evaluated for exhaustion four to eight weeks post-hospital discharge. Demographic and clinical data were obtained from self-report and medical chart review.

**Results**—Of the total sample (mean age 67.9±12.5, 90% male, 70% Caucasian, 3.12±1.3 grafts), approximately 41% reported exhaustion. When compared to their exhausted post-CABG counterpart, non-exhausted post-CABG patients had a significantly higher frequency of

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preoperative insulin use. Exhausted patients were significantly more likely to have higher left ventricular ejection fraction ([LVEF], *OR* 1.07, *p*=0.04), and elevated hemoglobin (*OR* 2.98, *p*=0.03) and eosinophils (*OR* 1.02, *p*=0.02) than those who were not exhausted.

**Conclusion**—Clinicians should evaluate all patients for exhaustion post-CABG surgery; patients with elevated LVEF, hemoglobin, and eosinophil levels warrant increased scrutiny.

### Keywords

Cardiac surgery; Coronary artery bypass graft; Predictors; Risk factors; Vital exhaustion

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## INTRODUCTION

Approximately 16.3 million Americans have coronary heart disease (CHD),<sup>1</sup> one of the leading causes of death and disability burden worldwide.<sup>2</sup> Fatigue is among the most common prodromal symptom in acute myocardial infarction.<sup>3–5</sup> The experience of fatigue has been documented weeks after coronary artery bypass graft (CABG) surgery, and associated with impaired psychosocial and physical functioning and decreased quality of life.<sup>6</sup> Vital exhaustion (hereafter referred to as exhaustion) is a psychological state characterized by extreme fatigue, lack of energy, general malaise, irritability, and demoralization, and is possibly related to numerous physiological variables.<sup>7</sup> Prevalence of exhaustion among those with CHD reportedly ranges from 35% – 75%.<sup>8, 9</sup> Exhaustion has been identified as an independent prognostic indicator of coronary artery disease morbidity and mortality with a two- to three-fold increase in future cardiac events (e.g. myocardial infarction, repeat revascularization, recurrent angina, and re-hospitalization).<sup>10, 11</sup>

Previous investigators have reported a variety of socio-demographic and clinical characteristics such as age, gender, race/ethnicity, socioeconomic status, education, body mass index, weight gain, smoking, diabetes, hypertension, and New York Heart Association classification as associated with exhaustion.<sup>12–15</sup> Individuals with higher exhaustion scores were more likely to be female<sup>11, 12</sup> and African American.<sup>16</sup> Surrogates of socioeconomic status (e.g. income, education) were significantly associated with exhaustion in patients with a history of CHD; individuals with low and middle income levels and elementary or high school education have a higher probability of becoming exhausted compared to those with high income or educational attainment beyond high school.<sup>17</sup> Several investigators also identified physiologic correlates of exhaustion including elevated inflammatory markers (e.g. interleukin-6, tumor necrosis factor-alpha, C-reactive protein);<sup>18–21</sup> suppression of cortisol;<sup>22</sup> abnormal lipid metabolism (e.g. elevated triglycerides and low levels of high-density lipoprotein);<sup>23, 24</sup> and impaired fibrinolytic activity (e.g. elevated fibrinogen and plasminogen activator inhibitor-1).<sup>25, 26</sup>

To our knowledge, only two studies by Boudrez and colleagues<sup>27, 28</sup> involved CABG patients, a population generally characterized by advanced age and high-grade, multivessel disease. In these two studies, the investigators examined the temporal change in exhaustion scores pre- and post-operatively. Boudrez et al.<sup>27</sup> observed significant gender differences, with women reporting higher pre-CABG exhaustion levels compared to men; these pre-CABG gender differences had disappeared by 4-months post-CABG. Findings from the

study by Boudrez and De Backer<sup>28</sup> revealed significant overall improvement in exhaustion scores between pre-CABG and six-months post-CABG. While these two studies constitute an important contribution to the literature on exhaustion, clinical and socio-demographic predictors of exhaustion in the CABG population have yet to be identified.

The aim of this descriptive, exploratory study was to determine whether preoperative socio-demographic and clinical variables were predictive of postoperative exhaustion in patients after CABG surgery. Discriminating between patients with exhaustion and non-exhaustion on the basis of clinical and socio-demographic factors may provide clinicians with insight for early assessment and secondary prevention strategies in order to attenuate disease progression and minimize future cardiac events. More importantly, findings may broaden our understanding of potential mechanisms by which exhaustion influences CHD and its adverse sequelae in the post-CABG population.

## METHODS

### Study Design and Sample

A descriptive, exploratory study design was conducted at two cardiac centers at a university-affiliated public healthcare institution and federal tertiary care facility. Subjects were a convenience sample of 42 patients (mean age  $67.9 \pm 12.54$ , 90% male, 70% Caucasian) who underwent CABG. Medical records were reviewed for eligibility criteria. Patients were included in the study if they were 45 years of age or older and underwent CABG surgery within the past four to eight weeks. Patients were excluded if they were clinically depressed; diagnosed with malignancy, autoimmune disorder, or active infection; a current smoker; were actively being treated for mood or affective disorders; or had postoperative complications (e.g. stroke, reoperation, sternal wound infections, pneumonia, readmission, and myocardial infarction) that would have influenced exhaustion within eight weeks of hospital discharge for CABG surgery.

### Procedures

The Institutional Review Board of the participating sites approved the study protocol, and all participants provided written informed consent. Data were collected by medical record review, patient interview, and written questionnaires. Participants underwent one study visit during morning hours in a location convenient for the patient (e.g. patient's home or outpatient clinic) for data collection between four to eight weeks post-hospital discharge. This time point was used to minimize the influence of wound healing as patients were more likely to have inflammatory profiles similar to their preoperative baseline levels.<sup>29</sup>

### Variables and Measures

**Depression Screening**—Patients were initially screened for the presence of depression disorder because of its potential overlap with exhaustion using the Patient Health Questionnaire-2.<sup>30</sup> Participants selected from among four responses for each item (not at all, several days, more than half the days, and nearly every day), and each response was scored as 0, 1, 2, and 3, respectively.<sup>30</sup> The Patient Health Questionnaire-2 scores can range from 0 to 6. The standard cut point of  $\geq 3$  to identify depression was utilized.<sup>30</sup> Sensitivity

and specificity for the Patient Health Questionnaire-2 is reportedly 83% and 90%, respectively, with a positive likelihood ratio of 2.9.<sup>30</sup> The questionnaire has been recommended for depression screening in the cardiovascular population by the interdisciplinary expert consensus of the National Heart, Lung, and Blood Working Group.<sup>31</sup>

**Exhaustion**—Participants were asked to complete the Maastricht Interview for Vital Exhaustion (MIVE), a 23-item standardized interview that measures the presence of exhaustion and includes questions regarding unusual fatigue, loss of energy, increased irritability, and feelings of demoralization.<sup>32</sup> Scores range from a minimum of 0 to a maximum of 23. In the current study, Cronbach's alpha for the MIVE was 0.85, indicating good reliability. Participants were designated as exhausted if they endorsed 7 out of 23 MIVE items.<sup>33</sup>

**Medical Record Review and Patient Interview**—A diverse group of socio-demographic and clinical variables were selected for study based on their theoretical relevance to the phenomenon of exhaustion (e.g.<sup>7, 17, 23, 34</sup>). Socio-demographic data, medical history, cardiovascular risk factors, and current medication regimen were collected by patient interview and verified by medical record review. The preoperative complete blood count was obtained by medical record review. Two trained researchers with experience in data abstraction and no prior knowledge of patients' exhaustion status independently reviewed patient medical records. Interrater reliability ( $\kappa$ ) was 0.95.

For socio-demographics, data were categorized as follows: gender (male vs. female); race/ethnicity (Caucasian vs. non-Caucasian); education (more than high school vs. high school or less); annual income (> \$40,000 vs. \$40,000); marital status (married or cohabitating vs. single, divorced, and widowed); and employment status (employed vs. retired and unemployed). For clinical characteristics, variables were defined as follows: cardiopulmonary bypass (off-pump vs. on-pump vs. combination) and procedural status (elective vs. emergent). Medical history, cardiovascular risk factors, coronary vessel involvement, and postoperative medications were dichotomized into no/yes categories. All other variables were reported as continuous data.

## Data Analysis

Descriptive statistics were used to summarize the sample data. T-test, chi-square or Fisher's Exact were used for between-group comparisons (exhausted vs. non-exhausted) of all socio-demographic and clinical predictor variables. Effect sizes were calculated using  $d$  and  $h$  estimates for respective mean and proportional group differences as established by Cohen:<sup>35</sup> 0.20 – 0.50 small, 0.50 – 0.80 moderate, and 0.80 large effect size. Multiple stepwise logistic regression was conducted to identify preoperative socio-demographic and clinical predictors with postoperative exhaustion status using entry criteria at 0.05 and elimination criteria at 0.10. Variables with a bivariate significance of  $p < 0.10$  were entered into the regression analyses to determine the best model of predictors for exhaustion. Variables included: age, gender, marital status, left ventricular ejection fraction (LVEF), body mass index, preoperative hemoglobin, hematocrit and eosinophils, diuretic use, insulin use, older

than 65 years of age, RCA disease, posterior lateral disease, previous angina, and valvular disease. Significance level was set at  $\alpha = 0.05$ . Log transformations were used to approximate normal distributions of hematologic data. All statistical analyses were performed using SPSS version 17 (SPSS, Inc., Chicago, Illinois).

## RESULTS

### Sample Socio-demographics and Clinical Characteristics

Socio-demographic and clinical characteristics of post-CABG patients with and without exhaustion are presented in Table 1 and Table 2. In the sample of 42 post-CABG patients with a mean age of 67.5 years, substantially more males and Caucasians were enrolled in the study than females and racial/ethnic minorities. On average, post-CABG patients underwent three bypass grafts. High-grade culprit atherosclerotic lesions in the left anterior descending artery as documented by prior cardiac angiography were most common followed by left main, left circumflex, and right coronary artery (RCA). Over half of the total sample had 3-vessel disease. The most frequent preoperative medical history included previous angina, valvular disease, myocardial infarction, and heart failure.

Seventeen patients (40.5%) were exhausted versus 25 (59.5%) who were not exhausted. Bivariate analyses revealed that both groups were comparable in terms of age, gender, race/ethnicity, marital status, and educational level. Exhausted subjects had higher LVEF and a non-significant trend toward higher body mass index. Interestingly, the presence of stenotic lesions in the posterior lateral artery was found to be significantly higher in the exhausted group compared to the non-exhausted group. There were no significant differences in the mean number of bypass grafts or diseased vessels, procedural status (elective vs. emergent) or cardiopulmonary bypass status (on-pump vs. off-pump vs. combination) as surrogates for surgical approach, and history of angina and valvular disease. Likewise, the prevalence of cardiovascular risk factors (premature family history of CHD, male gender, hypertension, hyperlipidemia, diabetes, smoking, alcohol use, and physical inactivity) was not significantly different among exhausted and non-exhausted subjects. There was a non-significant trend towards a higher frequency of patients older than 65 years in the non-exhausted group compared to the exhausted group. A significantly higher frequency of preoperative insulin users occurred in the non-exhausted group compared to the exhausted group; all other treatment regimens were similar in the two groups. Preoperative hemoglobin levels and eosinophil counts were higher in exhausted patients than non-exhausted patients, but the differences were not significant.

### Predictors of Exhaustion

Table 3 provides unadjusted univariate and multiple logistic regression analyses for predictors in the final model. In the univariate model, higher LVEF was significantly predictive of exhaustion compared to non-exhaustion. There was a non-significant trend towards higher eosinophil count and hemoglobin levels as increasing the odds of exhaustion as opposed to non-exhaustion. In the full model, both higher eosinophil concentration and hemoglobin were significant independent predictors of exhaustion, independent of LVEF. For every 1-unit increase in hemoglobin levels, the odds of being exhausted versus non-

exhausted were increased by a factor of 2.98. Additionally, the odds of post-CABG exhaustion were 2.1% greater with every 1-unit increase in preoperative eosinophil concentration than for those without exhaustion. There was negligible confounding in the effect of LVEF, hemoglobin, and eosinophils on exhaustion when adjusting for socio-demographic factors (age, gender, and marital status). Taken together, LVEF, hemoglobin level, and eosinophil count accounted for 59% of the variance in exhaustion.

## DISCUSSION

Our findings showed that 40.5% of the participants in our study were exhausted four to eight weeks after their CABG surgery. These findings are comparable to earlier studies that confirmed a moderately high level of exhaustion in both the pre- and post-operative CABG population.<sup>27, 28</sup> However, less is known about correlates of exhaustion in the CABG population. To our knowledge, this is the first study to identify clinical factors as independent predictors of postoperative CABG exhaustion. Patients with increases in LVEF, hemoglobin, and eosinophil count were more likely to be exhausted than were those without exhaustion. Notably, LVEF was found to be a significant predictor in the univariate but not multivariable analyses. Clinical factors were more robust predictors of exhaustion when compared to socio-demographic factors, which may be ascribed to the underlying pathophysiological mechanisms that mediate exhaustion with CHD and suggestive of the association between somatic symptoms and exhaustion as recently reported by Vroege, Zulkersma, and de Jonge.<sup>36</sup> In this sample of post-CABG patients, socio-demographic variables accounted for less than 3% of the variance when included in the final model, thereby providing a relatively small contribution in explaining exhaustion.

A counterintuitive finding in our study was that a significantly higher mean LVEF preoperatively was associated with exhaustion post-CABG. There was a 7% increase in the odds of post-CABG exhaustion versus non-exhaustion with increases in preoperative LVEF. In prior studies, the relationship between exhaustion and LVEF has been mixed with negative<sup>37, 38, 39</sup> and positive<sup>40</sup> results among individuals with CHD and heart failure. Our counterintuitive results might be best elucidated by two plausible explanations. First, our finding suggests that poor cardiac function in the preoperative period was not a predictor of exhaustion among individuals after CABG; in other words, post-CABG exhaustion may not be a consequence of dysfunctional cardiac pathology. This new finding of higher preserved left ventricular function among exhausted subjects may be the result of ischemic but viable myocardium and/or preoperative medication management (e.g. beta blockers).<sup>41</sup> The complexity of the relationship between increasing LVEF and exhaustion may involve various physiologic mechanisms not examined in this study. Secondly, the comorbidity of psychosocial factors such as lack of social support and hostility were unmeasured in this study, but may trigger mental stress. Mental stress has been shown to induce myocardial ischemia and is associated with decreased LVEF, and subsequent adverse clinical outcomes (e.g. mortality, myocardial infarction) in patients with CHD.<sup>42</sup> Although this relationship is unexpected, a paradoxical relationship has been previously described which supports further exploration of the relationship between LV function and exhaustion in a larger sample.

Normal but increasing levels of preoperative hemoglobin predicted exhaustion among post-CABG patients. We have no clear explanation for the association between hemoglobin and exhaustion; this finding will warrant further investigation. We were unable to ascertain whether higher hemoglobin levels were a consequence of increased red blood cell production. Elevated hemoglobin levels may be caused by conditions such as pulmonary disease, heart failure, polycythemia vera, and smoking. Both hemoglobin concentration and exhaustion were positively correlated with hematocrit levels in this study, and hemoglobin and hematocrit are among several factors that may influence blood viscosity.<sup>43</sup> Higher blood viscosity may compromise the blood's oxygen delivery by promoting red blood cell aggregation, reducing coronary blood flow, augmenting platelet and leukocyte adhesion to the endothelium, and increasing risk of thrombosis.<sup>44</sup> It remains to be determined whether our finding reveals an inflammatory-thrombotic pathway linking exhaustion to adverse cardiac outcomes.

We observed a novel association between preoperative absolute eosinophil count and postoperative exhaustion. Eosinophils account for approximately 1–4% of peripheral leukocytes, and are implicated in the immune response against parasitic infections, allergic disorders, tumors, and gastrointestinal disorders.<sup>45</sup> When activated, these granulated immune cells modulate innate and adaptive immunity through various mechanisms, which include the release of preformed biochemically active protein mediators and cytokines, antigen presentation, and phagocytosis. Although speculative, the link between exhaustion and eosinophils may be rooted in the recruitment of eosinophils by immunomodulators such as cytokines (e.g. IL-8).

Elevated eosinophils may reflect the pathological burden of atherosclerotic disease.<sup>46, 47, 48</sup> Recent evidence suggests that eosinophils play an important role in thrombus formation and coronary occlusion via coagulation and platelet activation pathways in acute coronary syndromes.<sup>49, 50</sup> Relationships between fatigue, depression and elevated eosinophil percentages have been reported in cancer research.<sup>51</sup> Interestingly, increased concentrations of eosinophil-selective chemokine, eotaxin, and eosinophil activation marker, eosinophil cationic protein, were observed in chronic fatigue syndrome and coronary atherosclerosis.<sup>52, 53</sup> This finding highlights a plausible immune-mediated inflammatory mechanism by which exhaustion may promote cardiovascular morbidity and mortality after cardiac surgery. Post hoc analyses did not reveal any correlation between eosinophils and cardiovascular risk factors or other comorbid diseases in the present study.

Another interesting finding was the statistically significant difference among exhausted and non-exhausted groups for preoperative insulin use. All eight subjects on insulin for diabetes were in the non-exhausted group. Hyperglycemia potentiates atherosclerosis progression through several mechanisms which includes indirectly activating NF- $\kappa$ B transcription of pro-inflammatory cytokine genes.<sup>54</sup> Exhaustion has been shown to be positively associated with glucose and insulin/glucose ratio.<sup>55</sup> Our finding is consistent with previous work demonstrating that insulin has significant anti-inflammatory effects. Insulin exerts its anti-atherogenic effects on the vessel wall by inducing endothelial nitric oxide synthase, which stimulates nitric oxide production, increases vascular blood flow, and attenuates pro-atherogenic intercellular adhesion molecule-1 upregulation, monocyte chemoattractant



protein-1 expression, and NF- $\kappa$ B signaling.<sup>56</sup> The anti-atherogenic effects of insulin may interfere with the pro-inflammatory and pro-atherogenic association that characterizes exhaustion. Hence, in the current study, non-exhausted status may be attributed to, in part, the anti-inflammatory effects of insulin.

### Limitations

Several limitations to our results should be acknowledged. The study sample was small; therefore, it is possible that a lack of statistical power undermined the ability to reveal significant differences and associations. In spite of a small sample size, effect sizes were large enough to detect reported differences and associations. Given the exploratory nature of this study, no corrections were applied to the alpha for multiple comparisons, which preserved power. Exact  $p$  values have been made available in order to draw inferences, which may include informal adjustments for multiple testing. Generalizability of the findings is limited; this study was conducted with a population of post-CABG patients that were highly educated and predominantly white with high household income levels. To determine whether the conclusion of this study is applicable and useful to more diverse CABG patients, further study in larger heterogeneous samples is warranted. There were no objective measures of functional status or New York Heart Association classification to correlate with exhaustion. Personality traits may influence exhaustion and warrant consideration in future analyses in addition to behavioral and psychosocial factors such as stress, anxiety, sleep, and physical activity. The results of the present study would benefit from confirmation in a larger sample, which would provide greater predictive power of the identified factors.

A couple of points are noteworthy. First, the timing of the assessment of exhaustion may be influenced by the presence of somatic symptoms following cardiac surgery. Previous investigators observed no significant difference in exhaustion levels before CABG or three to four weeks after CABG surgery;<sup>28</sup> however, such differences were observed at four months postoperatively.<sup>27</sup> We found no association between time since surgery and exhaustion. Second, although a proportionally shared variance has been reported between exhaustion and depression,<sup>57</sup> there are distinct conceptual differences. At the time of this study, evidence suggested that ‘depressed mood,’ and loss of self-esteem were virtually absent in exhausted patients.<sup>39</sup> Therefore, criteria to exclude depressed patients was used to remove the confounding influence of depression and increase the construct validity of the study; there were no exclusions by this process. Further study is required to tease out the relationship between depression and exhaustion.

### Conclusions

In summary, the association of exhaustion following CABG with higher preoperative LVEF, hemoglobin, and eosinophil concentrations is novel. While the findings do not establish causal associations, they may suggest complex physiologic pathways by which exhaustion exerts its influence in post-CABG patients. Clinicians should evaluate all patients for exhaustion post-CABG surgery; patients with elevated LVEF, hemoglobin, and eosinophil levels warrant increased scrutiny. Identifying preoperative risk factors for exhaustion may increase our ability to target patients in whom exhaustion may hamper surgical recovery.

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**Table 1**

Socio-demographic characteristics according to exhaustion status

Variable	Total Sample (n = 42) Mean ± SD	Exhaustion (n = 17) Mean ± SD	No Exhaustion (n = 25) Mean ± SD	P	ES (d)
Age	67.5±12.6	63.4 ± 9.5	70.1 ± 13.7	0.07	-0.54
<b>Gender</b>				0.08	
Male	38 (90)	17 (100)	21 (84)		0.82
Female	4 (10)	0	4 (16)		-0.82
<b>Race/Ethnicity</b>				0.37	
Caucasian	28 (67)	10 (59)	18 (72)		-0.27
Black	3 (7)	1 (6)	2 (8)		-0.08
Hispanic	2 (5)	2 (12)	0		0.71
Asian/Pacific Islander	9 (21)	4 (23)	5 (20)		0.07
<b>Education</b>				1.00	
More than High school	34 (83)	13 (81)	21 (84)		-0.08
High school or less	7 (17)	3 (19)	4 (16)		0.08
<b>Annual Income</b>				0.57	
\$20,000	8 (19)	3 (18)	5 (20)		-0.05
> \$20,000 – \$40,000	12 (29)	6 (35)	6 (24)		0.24
> \$40,000 – \$60,000	8 (19)	2 (12)	6 (24)		-0.32
> \$60,000	14 (33)	6 (35)	8 (32)		0.06
<b>Marital Status</b>				0.09	
Married or cohabitating	27 (64)	15 (88)	12 (48)		0.90
Divorced	1 (3)	0	1 (4)		-0.40
Widowed	8 (19)	1 (6)	7 (28)		-0.62
Single	6 (14)	1 (6)	5 (20)		-0.43
<b>Employment Status</b>				0.28	
Retired/Unemployed	24 (57)	8 (47)	16 (64)		-0.34
Employed	14 (33)	6 (35)	8 (32)		0.06
Self-employed	4 (10)	3 (18)	1 (4)		0.47

*d*, Cohen's *d*; ES, effect size; *h*, Cohen's *h*; SD, standard deviation.

\*  $p < 0.05$

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Table 2

Clinical characteristics by exhaustion status

Variable	Total Sample (n = 42) Mean ± SD	Exhaustion (n = 17) Mean ± SD	No Exhaustion (n = 25) Mean ± SD	P	ES (d)
LV Ejection Fraction (%)	52.61±12.5	57.9 ± 10.9	49.2 ± 12.5	0.03*	0.72
Body Mass Index	27.66±4.2	28.9 ± 4.3	26.8 ± 3.0	0.08	0.58
Highest Degree of Stenosis (%)	89.60±12.6	89.7 ± 12.4	89.5 ± 13.0	0.96	0.02
Total # of Bypass Grafts	3.12±1.3	3.5 ± 1.2	2.9 ± 1.3	0.15	0.47
<b>Preoperative Hematology</b>					
WBC (×1000/uL)	6.6±1.9	7.0 ± 2.1	6.3 ± 1.7	0.27	0.37
Lymphocytes (u/L)	1612.0±515.9	1672.7 ± 645.1	1564.3 ± 406.9	0.61	0.21
Neutrophils (u/L)	4051.72±1515.1	4316.7 ± 1428.2	3864.7 ± 1589	0.44	0.29
Monocytes (u/L)	531.03±167.1	516.7 ± 169.7	541.2 ± 169.8	0.71	-0.14
Eosinophils (u/L)	167.86±98.3	208.3 ± 99.6	137.5 ± 88.5	0.06	0.75
RBC (M/uL)	4.42±0.5	4.5 ± 0.5	4.3 ± 0.5	0.34	0.39
Hemoglobin (g/dL)	13.47±1.5	14.0 ± 1.6	13.1 ± 1.4	0.08	0.56
Hematocrit (%)	39.85±4.1	41.1 ± 4.3	39.0 ± 3.8	0.11	0.51
Platelets (k/uL)	232.48±50.7	231.6 ± 49.7	233.2 ± 53.0	0.93	-0.03
<b>Procedural Status</b>					
Elective CABG	36 (86)	14 (82.4)	22 (88)	0.67	-0.17
Emergent CABG	6 (14)	3 (17.6)	3 (12)		0.17
<b>Cardiopulmonary Bypass</b>					
On-pump	39 (93)	16 (94.1)	23 (92)	0.68	0.08
Off-pump	2 (5)	1 (5.9)	1 (4)		0.09
Combination On-pump/Off-pump	1 (2)	0	1 (4)		-0.40
<b>Cardiovascular Risk Factors</b>					
Family History of CAD	10 (24)	6 (35)	4 (16)	0.15	0.44
Hypertension	36 (86)	15 (88)	21 (84)	0.70	0.12



Variable	Total Sample (n = 42) Mean ± SD	Exhaustion (n = 17) Mean ± SD	No Exhaustion (n = 25) Mean ± SD	P	ES (d)
<b>Hyperlipidemia</b>	34 (81)	15 (88)	19 (76)	0.32	0.32
<b>Diabetes Mellitus</b>	23 (55)	10 (59)	13 (52)	0.66	0.14
<b>History of Tobacco Use</b>	29 (69)	14 (82)	15 (60)	0.12	0.49
<b>Age &gt; 65 years</b>	20 (48)	5 (29)	15 (60)	0.05	-0.64
<b>Physical Inactivity</b>	31 (74)	13 (77)	18 (72)	0.39	0.12
<b>Medications</b>					
<b>Aspirin</b>	38 (91)	16 (94)	22 (88)	0.51	0.21
<b>Clopidigrel</b>	19 (45)	9 (53)	10 (40)	0.41	0.26
<b>ACE Inhibitors</b>	17 (41)	8 (47)	9 (36)	0.47	0.22
<b>Beta Blockers</b>	40 (95)	17 (100)	23 (92)	0.23	0.57
<b>Statins</b>	38 (91)	15 (88)	23 (92)	0.68	-0.13
<b>Diuretics</b>	33 (79)	11 (65)	22 (88)	0.07	-0.56
<b>Nitrates</b>	6 (14)	3 (18)	3 (12)	0.61	0.17
<b>Insulin</b>	8 (19)	0	8 (32)	0.01*	-0.90
<b>Oral Hypoglycemic Agents</b>	14 (33)	6 (35)	8 (32)	0.82	0.06
<b>CAD Vessel Involvement</b>					
<b>Left Main</b>	13 (31)	5 (29)	8 (32)	0.86	-0.07
<b>Left Anterior Descending</b>	39 (93)	17 (100)	22 (88)	0.14	0.71
<b>Circumflex</b>	29 (69)	13 (77)	16 (64)	0.39	0.29
<b>Right Coronary Artery</b>	28 (67)	14 (82)	14 (56)	0.08	0.57
<b>Posterior Lateral</b>	3 (7)	3 (18)	0	0.03*	0.88
<b>Preoperative Medical Hx</b>					
<b>Myocardial Infarction</b>	14 (33)	6 (35)	8 (32)	0.82	0.06
<b>Angina</b>	25 (60)	13 (77)	12 (48)	0.07	0.61
<b>Heart Failure</b>	7 (17)	2 (12)	5 (20)	0.32	-0.22
<b>Valvular Disease</b>	17 (41)	4 (24)	13 (52)	0.06	0.59

ACE, angiotensin-converting enzyme; CABG, coronary artery bypass graft; CAD, coronary artery disease; d, Cohen's d; ES, effect size; h, Cohen's h; Hx, history; LV, left ventricular; RBC, red blood count; SD, standard deviation; WBC, white blood count.

\* p < 0.05

**Table 3**

Logistic regression analyses to identify predictors of exhaustion risk (n=41)

	Univariate Logistic Regression Model		Multiple Logistic Regression Model <sup>a</sup>			
	OR	95% CI	P	OR	95% CI	P
LVEF (%)	1.067	1.067 – 1.136	0.039	1.118	0.990 – 1.263	0.070
Eosinophil Count (/uL)	1.008	0.999 – 1.018	0.070	1.021	1.004 – 1.038	0.015
Hemoglobin (g/dL)	1.488	0.945 – 2.343	0.086	2.978	1.097 – 8.085	0.032

<sup>a</sup>Multiple Logistic Regression Model (unadjusted): Model  $\chi^2 = 15.54$ , df 3,  $P = 0.001$ ; Hosmer–Lemeshow statistic:  $\chi^2 = 3.33$ , df 7,  $P = 0.85$ , Nagelkerke  $R^2 = 0.59$

Independent variables were continuous.

CI, confidence interval; df, degrees of freedom; OR, odds ratio; SE, standard error; LVEF, left ventricular ejection fraction.