Research Article

Preoperative White Blood Cell Count and Risk of 30-Day Readmission after Cardiac Surgery

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1. Introduction

Approximately one in every five hospitalized patients is readmitted within 30 days of discharge [1]. Currently, two-thirds of US hospitals have reimbursement penalties for higher than expected 30-day readmission rates from the Center for Medicaid and Medicare Services [2, 3]. It is expected that similar penalties will be extended to other procedures and diagnoses including cardiac surgery. In preparation for the expansion of the penalty system in the USA and to improve prediction of patients at high risk of postdischarge complications leading to readmissions or premature death, risk factors must be
identified early in the hospital course to align the best possible quality and continuity of care.

Currently, a validated risk model for predicting readmissions after cardiac surgery is not available and few risk factors for readmission are known. Recent evidence from California reported an association between infection and higher rates of 30-day readmission after cardiac surgery [4]. However, identification of infection after discharge without routine monitoring of a postcardiac surgical patient is problematic. What is needed is for clinical care teams to identify patients at high risk of infection before cardiac surgery to determine readiness and safety for the patient to undergo surgery. A common marker of inflammation is white blood cell (WBC) count, routinely measured prior to cardiac surgery. WBC count provides a broad measure of inflammation status, whether as a result of infection or proinflammatory disease states such as diabetes, COPD, or hemodialysis [5–8]. Elevated WBC count is reported as a component of the systemic inflammatory response syndrome (SIRS) to sepsis and is endorsed as a marker for reporting the systemic inflammatory response to cardiopulmonary bypass [9, 10]. In addition, current evidence has shown that preoperative WBC count is predictive of in-hospital mortality and stroke [11] and major bleeding [12] after coronary artery bypass graft surgery and associated with complications in other endovascular and thoracic procedures [13, 14], suggesting that preoperative WBC count may aid clinical care teams in risk-stratifying patients prior to surgery. However, it is not known if a patient’s baseline inflammatory state measured by crude WBC count could predict 30-day readmission. Therefore, we sought to evaluate whether preoperative WBC count was associated with 30-day readmissions after cardiac surgery.

2. Methods

Patients undergoing coronary artery bypass graft (CABG) surgery and/or valve surgery within the Northern New England Cardiovascular Disease Study Group (NNE) between July 2008 and December 2010 were enrolled in the cohort. A total of 2,209 consecutive patients were included along with 268 readmissions to the hospital performing the index cardiac surgery. Twelve patients were excluded due to missing white blood cell counts and twenty-one for incomplete data, leaving a total of 2,176 patients and 259 readmissions occurring within 30 days of discharge from the index cardiac surgery admission. All institutional review boards for each center reviewed and approved the data collection for the NNE registry and supplementary data collection for readmissions.

The NNE is a voluntary regional consortium of physicians, allied health professionals, research scientists, and hospital administrators from institutions in Maine, New Hampshire, and Vermont that support coronary revascularization and open-heart surgery. The goal of the consortium is to foster continuous improvement in the quality, safety, and effectiveness of care for patients with cardiovascular disease through the analysis of process and outcomes data with timely feedback to the health care professionals providing these services. All the hospitals providing open-heart surgery in this region contribute data on consecutive cases with validation of procedure numbers and mortality performed every two years. The registry collects data on patient characteristics, procedural indication, priority, and process, and in-hospital outcomes (see http://www.nnecdsg.org/ for the data forms and publically available data).

WBC count was defined as the last preoperative measurement of WBC taken prior to procedure, was collected by data abstractor at each center. Categories of WBC counts were

| Table 1: Characteristics of patients with or without 30-day readmission. |
|-------------------------------------------------|
| Characteristic | No | Yes | P value |
| Number of patients (2,176) | 1,917 | 259 |
| Demographics | | | |
| Age | 66.2 ± 11.2 | 66.4 ± 11.5 | 0.740 |
| Female | 28.5 | 32.8 | 0.154 |
| BMI | 29.6 ± 5.9 | 29.8 ± 6.5 | 0.585 |
| Comorbidities | | | |
| Type 2 diabetes mellitus | 31.5 | 37.1 | 0.070 |
| Vascular disease | 27.3 | 30.9 | 0.224 |
| COPD | 15.6 | 20.5 | 0.043 |
| History of dialysis | 2.4 | 5.0 | 0.015 |
| Smoking | 21.4 | 22.4 | 0.726 |
| Cardiac history | | | |
| Recent MI | 17.3 | 13.1 | 0.091 |
| CHF | 19.9 | 25.1 | 0.051 |
| Prior CABG | 3.9 | 2.7 | 0.337 |
| Prior valve | 1.5 | 1.9 | 0.611 |
| Prior PCI | 18.2 | 17.4 | 0.760 |
| NYHA Class IV | 15.6 | 15.4 | 0.949 |
| Cardiac anatomy and function | | | |
| Left main disease ≥50% | 28.8 | 20.9 | 0.007 |
| Single-vessel disease | 33.5 | 42.6 | 0.002 |
| Two-vessel disease | 28.5 | 30.2 |
| Three-vessel disease | 38.1 | 27.3 |
| Ejection fraction | | | |
| <40% | 11.3 | 12.3 | 0.894 |
| 40%–59% | 12.6 | 11.1 |
| 50%–59% | 24.3 | 24.2 |
| ≥60% | 51.7 | 52.4 |
| White blood cell count (in 1,000's, mm³) | | | |
| <6.0 | 19.9 | 19.7 | 0.037 |
| 6.0–7.9 | 39.2 | 35.9 |
| 8.0–9.9 | 25.3 | 21.6 |
| 10.0–12.0 | 9.9 | 13.1 |
| >12.0 | 5.6 | 9.7 |

COPD: chronic obstructive pulmonary disease; MI: myocardial infarction; CHF: congestive heart failure; CABG: coronary artery bypass graft surgery; PCI: percutaneous coronary intervention; WBC: white blood cell; eGFR: estimated glomerular filtration rate.
Table 2: Procedural characteristics and outcomes of patients with or without 30-day readmission.

| Characteristic                              | 30-day readmission |
|--------------------------------------------|--------------------|
|                                            | No     | Yes    | P value |
| Procedural characteristics                |        |        |         |
| Priority                                   |        |        |         |
| Emergent                                  | 5.3    | 6.6    | 0.534   |
| Urgent                                    | 50.9   | 47.9   |         |
| Elective                                  | 43.9   | 45.6   |         |
| Procedure                                 |        |        |         |
| CABG                                      | 60.7   | 51.0   | 0.007   |
| Valve                                     | 22.4   | 30.1   |         |
| CABG/valve                                | 17.0   | 18.9   |         |
| On-pump surgery                           | 90.3   | 95.8   | 0.004   |
| Nadir hematocrit < 20 on bypass            | 15.0   | 20.5   | 0.029   |
| Cardiopulmonary bypass time (min)         | 119.7 ± 53.7 | 122.9 ± 56.5 | 0.393 |
| Time to initial extubation (min)           | 17.3 ± 65.2 | 17.6 ± 35.1 | 0.951   |
| Intraoperative myocardial infarction       | 2.4    | 2.7    | 0.725   |
| Return to bypass                          | 4.2    | 4.6    | 0.730   |
| Management                                |        |        |         |
| RBC transfusions                          |        |        |         |
| None                                      | 67.6   | 58.7   | 0.001   |
| One                                       | 8.9    | 10.0   |         |
| Two                                       | 10.3   | 9.3    |         |
| Three or more                             | 13.2   | 22.0   |         |
| Use of 1 or more inotropes                |        |        |         |
| Arrive to ICU                             | 43.9   | 44.0   | 0.965   |
| After 4 hours                             | 37.2   | 44.0   | 0.034   |
| After 48 hours                            | 11.3   | 15.1   | 0.080   |
| Adverse outcomes                          |        |        |         |
| Low-cardiac output failure                 | 8.0    | 10.0   | 0.272   |
| Stroke                                    | 1.1    | 1.5    | 0.525   |
| Mediastinitis                             | 0.4    | 2.7    | <0.001  |
| Acute kidney injury                       | 30.7   | 49.4   | <0.001  |
| Reintubation                              | 3.7    | 3.9    | 0.866   |
| Return to operating room for bleeding     | 3.2    | 4.3    | 0.395   |
| New atrial fibrillation                   | 32.6   | 39.8   | 0.021   |
| Leg wound infection                       | 0.7    | 1.2    | 0.463   |
| Pneumonia                                 | 1.7    | 0.8    | 0.275   |

CABG: coronary artery bypass graft surgery; RBC: packed red blood cell transfusion; ICU: intensive care unit.

divided into predefined categories (<6.0, 6.0–7.9, 8.0–9.9, 10.0–12.0, and >12.0 thousands per cubic millimeter, mm$^3$).

Baseline, operative, and postoperative outcomes were compared using chi-square tests and continuous data using Student’s t-test or Wilcoxon rank sum tests where appropriate. We conducted both univariate and backwards stepwise logistic regression removing risk factors that did not reach an alpha <0.1 among only risk factors with an alpha <0.1 from univariate comparisons. All risk factors meeting an alpha <0.1 were included in the final model multivariate logistic regression model. Categories of white blood cell counts were then added to the multivariate clinical risk prediction model. We conducted a Hosmer-Lemeshow goodness of fit test and calculated the area under the receiver operating characteristic (ROC) curve for the final multivariate model with categories of white blood cell count and reported the ROC and 95% confidence intervals for each model. All analyses were performed using Stata 11.2 (College Station, TX).

3. Results

Among the 2,176 patients, 259 patients were readmitted within 30 days (11.9%). The median time of readmission was 9 (IQR 4–16) days. Patient demographics were similar between patients with a 30 day readmission and those without a readmission. Patients readmitted within 30 days were more likely to have chronic obstructive pulmonary disease,
Table 3: Univariate and multivariate regression analysis for 30-day readmission.

| White blood cell count (in 1,000’s, mm$^3$) | Univariate Odds ratios (95% CI) | Multivariate Odds ratios (95% CI) |
|--------------------------------------------|-------------------------------|---------------------------------|
| < 6.0                                      | Reference                     | Reference                       |
| 6.0–7.9                                    | 0.93 (0.64, 1.33)              | 0.96 (0.65, 1.41)               |
| 8.0–9.9                                    | 0.86 (0.58, 1.29)              | 0.91 (0.59, 1.39)               |
| 10.0–12.0                                  | 1.34 (0.84, 2.14)              | 1.42 (0.86, 2.34)               |
| >12.0                                      | 1.73 (1.03, 2.93)              | 1.81 (1.03, 3.17)               |

Other risk factors

| Factor                              | Univariate Odds ratios (95% CI) | Multivariate Odds ratios (95% CI) |
|-------------------------------------|---------------------------------|---------------------------------|
| Single-vessel disease               | 1.77 (1.28, 2.46)               | 1.73 (1.24, 2.43)               |
| Two-vessel disease                  | 1.48 (1.04, 2.10)               | 1.43 (1.00, 2.06)               |
| On-pump surgery                     | 2.43 (1.31, 4.54)               | 1.85 (0.98, 3.52)               |
| Nadir hematocrit on bypass < 20     | 1.55 (1.10, 2.17)               | 1.39 (0.96, 2.00)               |
| Three or more packed red blood cells| 1.86 (1.34, 2.56)               | 1.52 (1.07, 2.18)               |
| Mediastinitis                       | 7.58 (2.64, 21.79)              | 5.81 (1.87, 18.08)              |
| Acute kidney injury                 | 2.21 (1.70, 2.87)               | 2.03 (1.53, 2.68)               |

Model parameters

| Hosmer-Lemeshow $\chi^2$, $P$ value |
|-------------------------------------|
| $\chi^2 = 10.94$, $P$ value = 0.2  |

| ROC   |
|-------|
| 0.66  |

WBC: white blood cell; SD: standard deviation of the log-transform of WBC count; ROC: area under the receiver operating characteristic curve.

Figure 1: Preoperative White Blood Cell Counts and Risk of 30-day Readmission. The graph plots the risk of all-cause 30-day readmission by five pre-defined categories of preoperative white blood cell counts (in thousands per cubic millimeter, mm$^3$).

4. Discussion

We explored the predictive ability of WBC counts prior to cardiac surgery on 30-day readmission. With and without adjustment of other risk factors for readmission, patients with preoperative WBC counts >12,000 (mm$^3$) were significantly more likely to be readmitted to the hospital within 30 days from discharge. We are the first to demonstrate that a marker of inflammation prior to the start of surgery demonstrates increased risk of 30-day readmission and should be incorporated into risk models to predict readmission prior to discharge from cardiac surgery.

WBC count has enjoyed a resurgence in recent years as a valid marker of inflammation and as a strong independent predictor of future coronary heart disease and stroke [15, 16]. After an acute event, patient outcomes remain influenced by WBC count at the time of hospital admission. In several studies, peak WBC count or elevated monocyte count has been
### Table 4: Characteristics of patients and white blood cell count categories.

| Characteristic                              | <6.0  | 6.0–7.9 | 8.0–9.9 | 10.0–12.0 | >12.0 | P value |
|---------------------------------------------|-------|---------|---------|-----------|-------|---------|
| Number of patients (2,176)                  | 433   | 845     | 541     | 224       | 133   |         |
| Demographics                                |       |         |         |           |       |         |
| Age                                         | 67.7 ± 11.3 | 67.1 ± 10.6 | 65.5 ± 11.4 | 63.6 ± 11.7 | 63.5 ± 12.1 | <0.001 |
| Female                                      | 30.3  | 29.5    | 26.6    | 31.7      | 27.8  | 0.594   |
| BMI                                         | 28.5 ± 5.3 | 29.6 ± 6.0 | 30.3 ± 6.2 | 30.3 ± 6.1 | 29.4 ± 5.5 | <0.001 |
| Comorbidities                               |       |         |         |           |       |         |
| Type 2 diabetes mellitus                    | 26.3  | 31.6    | 36.8    | 32.6      | 34.6  | 0.014   |
| Vascular disease                            | 25.6  | 27.9    | 27.9    | 29.9      | 28.6  | 0.817   |
| COPD                                        | 12.2  | 14.7    | 19.4    | 20.1      | 18.1  | 0.009   |
| History of dialysis                         | 2.1   | 2.4     | 2.6     | 2.7       | 7.5   | 0.013   |
| Smoking                                     | 9.7   | 17.9    | 28.8    | 35.7      | 30.1  | <0.001  |
| Cardiac history                             |       |         |         |           |       |         |
| Recent MI                                   | 7.6   | 15.5    | 17.6    | 28.1      | 33.1  | <0.001  |
| CHF                                         | 18.7  | 18.7    | 21.4    | 22.3      | 30.8  | 0.017   |
| Prior CABG                                  | 5.1   | 3.9     | 3.1     | 1.8       | 4.5   | 0.256   |
| Prior valve                                 | 2.5   | 1.3     | 0.9     | 1.3       | 3.0   | 0.173   |
| Prior PCI                                   | 15.9  | 18.6    | 19.2    | 17.0      | 18.8  | 0.699   |
| NYHA Class IV                               | 12.0  | 12.2    | 16.6    | 24.6      | 29.3  | <0.001  |
| Cardiac anatomy and function                |       |         |         |           |       |         |
| Left main disease ≥50%                      | 22.9  | 27.9    | 27.9    | 31.3      | 37.6  | 0.012   |
| Single-vessel disease                       | 41.6  | 34.7    | 33.0    | 28.1      | 26.8  | 0.013   |
| Two-vessel disease                          | 27.5  | 28.2    | 28.8    | 32.9      | 28.5  |         |
| Three-vessel disease                        | 30.9  | 37.2    | 38.2    | 39.1      | 44.7  |         |
| Ejection fraction                           |       |         |         |           |       |         |
| <40%                                        | 9.4   | 9.3     | 12.0    | 15.0      | 22.8  | <0.001  |
| 40%–59%                                     | 11.1  | 10.9    | 14.1    | 18.2      | 9.5   |         |
| 50%–59%                                     | 25.9  | 24.2    | 24.1    | 21.5      | 26.0  |         |
| ≥60%                                        | 53.5  | 55.5    | 49.8    | 45.3      | 41.7  |         |
| Procedural characteristics                  |       |         |         |           |       |         |
| Priority                                    |       |         |         |           |       |         |
| Emergent                                    | 1.6   | 2.8     | 6.1     | 10.3      | 23.3  | <0.001  |
| Urgent                                      | 46.0  | 47.9    | 51.2    | 61.2      | 60.9  |         |
| Elective                                    | 52.4  | 49.2    | 42.7    | 28.6      | 15.8  |         |
| Procedure                                   |       |         |         |           |       |         |
| CABG                                        | 50.6  | 59.1    | 62.5    | 67.4      | 66.2  | <0.001  |
| Valve                                       | 31.4  | 23.7    | 21.3    | 15.2      | 16.5  |         |
| CABG/valve                                  | 18.0  | 17.3    | 16.3    | 17.4      | 17.3  |         |
| On-pump surgery                             | 92.4  | 92.0    | 88.7    | 89.7      | 90.2  | 0.213   |
| Nadir hematocrit < 20 on bypass             | 11.8  | 15.0    | 13.7    | 12.1      | 15.8  | 0.465   |
| Cardiopulmonary bypass time (min)           | 121.5 ± 55.2 | 117.1 ± 49.2 | 122.1 ± 55.7 | 121.4 ± 62.2 | 124.7 ± 57.9 | 0.656 |
| Time to initial extubation (min)             | 14.4 ± 28.6 | 15.6 ± 32.7 | 16.6 ± 51.4 | 20.8 ± 51.8 | 35.9 ± 199.8 | <0.001 |
| Intraoperative myocardial infarction        | 1.2   | 2.5     | 2.4     | 3.1       | 4.5   | 0.203   |
| Return to bypass                            | 5.1   | 4.7     | 3.0     | 3.1       | 5.3   | 0.343   |
| Management                                  |       |         |         |           |       |         |
| RBC transfusion                             | 36.3  | 32.9    | 30.7    | 31.7      | 43.6  | 0.041   |
| Use of 2 or more inotropes within 48 hours   | 2.1   | 3.6     | 2.5     | 4.5       | 4.6   | 0.278   |
linked to death or major adverse cardiac events (MACEs) outcomes, including readmission [17–19]. Other strong evidence has linked high WBC count at admission with adverse outcomes (mortality and bleeding) in patients undergoing coronary revascularization with cardiopulmonary bypass [11, 12]. However, in the case of cardiopulmonary bypass it is unclear whether high WBC count contributes to preexisting risk or to development of the systemic inflammatory response postoperatively or both.

The systemic inflammatory response is a complication in cardiopulmonary bypass patients that is caused by a combination of surgical stress and contact activation of blood component in the extracorporeal circuit [20, 21]. It is poorly defined [22] and the only formal definition is the Systemic Inflammatory Response Syndrome (SIRS), borrowed from the sepsis field [9]. According to the definition, SIRS exists when any two out of four criteria relating to abnormal temperature, heart rate, respiratory rate, or white cell counts exist. The upper threshold for abnormal white cell count according to the definition is 12,000 [9]. An evidence-based review of the inflammatory response indicated that all four SIRS criteria were rarely monitored in the setting of cardiopulmonary bypass [23] as they were felt to be too nonspecific [22] and if taken literally would apply to approximately 40% of all patients [24–26]. A more recent update on minimal reporting criteria by the Outcomes Consensus Panel singled out WBC count as the only criterion measured on its own as being relevant to the inflammatory status [10]. This recommendation was supported by other fields in which WBC count is recognized as a valid marker of inflammation [5, 6, 8, 27].

An alternative theory for the development of the systemic inflammatory response is that this is determined less by the extracorporeal circuit itself but rather by preexisting activation of white cells and endothelium [28] or by preoperative transfusion. Consistent with this theory is that high WBC count prior to coronary surgery utilizing cardiopulmonary bypass is linked with adverse outcomes including mortality and bleeding [11, 12]. Our present findings that high WBC count before surgery is linked to an increased risk of 30-day readmission after discharge add further weight to this idea.

We therefore conclude that WBC count measured prior to cardiac surgery may serve as a measure of the patient’s inflammatory status and could aid in identifying and managing patients at heightened risk of readmission after discharge from cardiac surgery. This becomes especially relevant in an era when higher than expected readmission rates may attract financial penalties to hospitals.

Conflict of Interests

The authors declare no conflict of interests.

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