# Blood Management and Infections in Cardiovascular and Orthopedic Surgery

Aryeh Shander, M.D., Cynthia Walawander, M.A., and the Blood Management Demonstration Group

## ABSTRACT

**Objectives.** Numerous risks are associated with allogeneic blood transfusions. Various blood management techniques have evolved which minimize or eliminate the use of allogeneic blood. This study compared infection rates associated with blood management techniques in patients undergoing cardiac and orthopedic surgeries where anticipated blood loss exceeds 1,000 mL.

**Methods.** Patients were enrolled at nine hospitals. Postoperative infection rate (to patient discharge) was compared between patients receiving allogeneic (includes allogeneic, +/- autologous, +/- reinfused blood and volume replacement) and other (non-allogeneic and/or volume replacement) transfusions. Relative risk and 95% confidence intervals were calculated to compare infection rates. Statistical significance was defined as $p < 0.05$.

**Results.** The overall infection rate was 5.8%; 2.2% for orthopedic patients and 13.9% for cardiac patients. The infection types included: pneumonia (n=21), sepsis (n=4), urinary tract infection (n=24), incisional wound infection (n=17), catheter associated infection (n=4), osteomyelitis (n=1), cardiovascular infection (n=2), other (n=20). Overall, the relative risk (95% CI) of post-operative infection was 3.6 (2.4, 5.4, p=0.001) times greater in the allogeneic group. When separated by surgery type, the relative risk of infection with allogeneic transfusion (95% CI) was 1.9 (0.8, 4.8, p=0.164) in orthopedic patients and 1.9 (1.1, 3.1, p=0.014) in cardiac patients.

**Conclusions.** Overall, an increased risk of postoperative infection associated with receipt of allogeneic blood was observed; a similar trend was observed when cardiac and orthopedic patients were separately considered.

## INTRODUCTION

- Blood loss with major elective surgery can be substantial and often requires perioperative transfusion with allogeneic or autologous blood.
- Specific risks associated with allogeneic blood transfusions include the transmission of blood-borne infections and immunomodulatory effects.
- Experimental and epidemiologic observations indicate that allogeneic transfusions are associated with an increased prevalence of postoperative bacterial infections.
- A number of autologous blood options can potentially reduce or eliminate the need for allogeneic blood.
- This study compared the infection rates associated with blood management techniques in patients undergoing cardiac and orthopedic surgeries where blood loss was anticipated to exceed 1000 mL.

## OBJECTIVE

- To compare the post-operative infection rate in patients undergoing major orthopedic and cardiac surgeries utilizing allogeneic versus non-allogeneic blood management.

## METHODS

### Study Design

- Observational, sequential sampling design study conducted at nine community hospitals.
- Standard data collection form used to record: demographic information, pre-existing medical conditions/risk factors (categorized by cardiovascular, endocrine, gastrointestinal, hepatic, renal, hematology/oncology, social history, respiratory, neurologic, surgical, and other), medical history, medication history, perioperative times, surgical and anesthesia procedures, blood transfusion and volume replacement information, and postoperative infections.
- Protocol received IRB approval and informed consent was obtained prior to patient enrollment.

### Inclusion Criteria

- In-patient surgeries including: total or partial hip replacement/revision, total knee replacement/revision, shoulder arthroplasty, coronary artery bypass graft, replacement of any heart valve (with prosthesis/tissue graft), and thoracic vessel resection with replacement.

### Exclusion Criteria

- Age < 18 years, immunocompromised from current malignancy, systemic viral or bacterial infection, trauma requiring multiple surgeries, or incompetent to provide consent.

### Blood Management Definitions

- Allogeneic: transfusion of donor-supplied red blood cells, plasma, platelets, or cryoprecipitate with/without receipt of other blood management techniques.
- Other: autologous blood transfusions and/or CT autotransfusions, orthopedic autotransfusions, cell salvage, or ANH and/or volume replacement with colloids and/or crystalloids.

### Clinical Outcome: Post-Operative Infection Rate

- Infections included pneumonia, sepsis, UTI, incisional or deep surgical wound infection, catheter-associated infection, osteomyelitis, septic arthritis, and cardiovascular infection (all as defined by CDC), and other infections defined by the primary investigator that occurred between the time of surgery until hospital discharge.

### Statistical Methods

- Statistical analysis performed using SAS® software.
- Blood management comparisons performed using chi-square or Fisher exact test for categorical variables, and t-tests or Wilcoxon rank-sum tests for continuous variables.
- Logistic regression analysis assessed influence of blood management technique and other patient factors on postoperative infection risk.
- Univariate model – factors tested included: demographic factors, pre-existing medical conditions, blood management technique, surgery type.
- Model fit assessment: Hosmer-Lemeshow GOF test, area under the ROC curve, and overall precision of the estimates.

## RESULTS

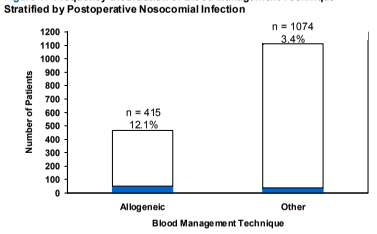
- Data were obtained from 1489 patients (455 cardiovascular, 1034 orthopedic). There were 415 and 1074 patients in the allogeneic and other groups respectively. The mean (SD) age was 65.6 (11.7); 49% were male, 80% were Caucasian, and 38, 42, and 18% were in ASA class 2, 3, and 4, respectively.

**Table 1: Demographic Characteristics Stratified by PostOperative Nosocomial Infection**

| Demographic Characteristic | Postoperative Nosocomial Infection | | p-value | Relative Risk | 95% Confidence Interval |
|---|---|---|---|---|---|
| | No | Yes | | | |
| Age (year) | | | | | |
| Number of Patients | 1403 | 86 | 0.0042 | 1.03 | (1.02, 1.05) |
| Mean (SD) | 65.4 (11.7) | 69.0 (11.2) | | | |
| Median | 67 | 71 | | | |
| Minimum-Maximum | 22-94 | 38-89 | | | |
| Weight (kg) | | | | | |
| Number of Patients | 1403 | 86 | 0.1430 | | |
| Mean (SD) | 86.9 (21.0) | 82.9 (20.9) | | | |
| Median | 85 | 83 | | | |
| Minimum-Maximum | 28-186 | 31-138 | | | |
| Body Mass Index (kg/m$^2$) | | | | | |
| Number of Patients | 1399 | 86 | 0.1679 | 0.97 | (0.94, 1.01) |
| Mean (SD) | 30.3 (6.9) | 29 (6.9) | | | |
| Median | 29 | 28 | | | |
| Minimum-Maximum | 10-58 | 10-46 | | | |
| Gender | | | | | |
| Females, n (%) | 715 (93.6%) | 49 (6.4%) | 0.279 | 1.3 | (0.8, 1.9) |
| Males, n (%) | 688 (94.9%) | 37 (5.1%) | | | |
| Blood Management Technique | | | 0.001 | 3.6 | (2.4, 5.4) |
| Allogeneic, n (%) | 365 (87.6%) | 50 (12.1%) | | | |
| Other[1], n (%) | 1038 (96.7%) | 36 (3.4%) | | | |
| Surgery Type | | | | | |
| Cardiovascular, n (%) | 392 (86.2%) | 63 (13.9%) | 0.001 | 6.2 | (3.9, 9.9) |
| Orthopedic, n (%) | 1011 (97.8%) | 23 (2.2%) | | | |
| Race | | | | | |
| Caucasian, n (%) | 1123 (94.0%) | 72 (6.0%) | 0.406 | 1.3 | (0.7, 2.2) |
| Other, n (%) | 280 (95.2%) | 14 (4.8%) | | | |
| ASA Class | | | | | |
| ≥ 4, n (%) | 235 (85.1%) | 41 (14.9%) | 0.001 | 1.1 | (1.07, 1.19) |
| ≤ 3, n (%) | 1168 (96.3%) | 45 (3.7%) | | | |

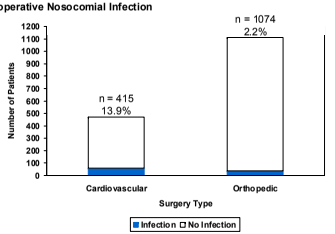
[1] Other refers to both non-allogeneic blood transfusion and volume replacement combined.

**Figure 1: Frequency Distribution of Blood Management Technique Stratified by Postoperative Nosocomial Infection**




Top number above bar represents number of patients in specified blood management technique.
Bottom number represents percentage of patients experiencing a post-op nosocomial infection.

**Figure 2: Frequency Distribution of Surgery Type Stratified by Postoperative Nosocomial Infection**




Top number above bar represents number of patients in specified surgery type.
Bottom number represents percentage of patients experiencing a post-op nosocomial infection.

- Overall, the relative risk (95% CI) of postoperative infection was 3.6 (2.4, 5.4) times greater in the allogeneic group. When separated by surgery type, the relative risk of infection with allogeneic transfusion (95% CI) was 1.9 (0.8, 4.8) in orthopedic patients (p=0.164) and 1.9 (1.1, 3.1) in cardiac patients (p=0.014).

**Table 2: Occurrences of Postoperative Nosocomial Infections Stratified by Blood Management Technique**

| Post-Operative Infection | Blood Management Technique | |
|---|---|---|
| | Allogeneic Transfusion (n=415) | Other (n=1,074) |
| Pneumonia | 14 (3.4%) | 7 (0.7%) |
| Sepsis | 1 (0.24%) | 3 (0.28%) |
| Urinary Tract Infection | 12 (2.89%) | 12 (1.12%) |
| Incisional Surgical Wound Infection | 14 (3.37%) | 3 (0.28%) |
| Deep Surgical Wound Infection | 2 (0.48%) | 0 |
| Catheter Associated Infection | 4 (0.96%) | 0 |
| Osteomyelitis | 0 | 1 (0.09%) |
| Septic Arthritis | 0 | 0 |
| Cardiovascular | 0 | 2 (0.19%) |
| Other[2] | 8 (1.93%) | 10 (0.93%) |

[1] Other refers to both non-allogeneic blood transfusion and volume replacement combined.
[2] Patients may have had two infection types recorded.

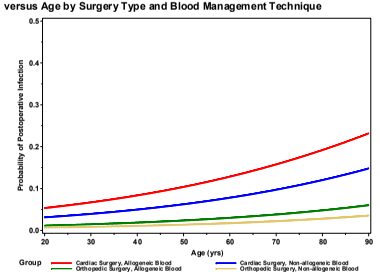
Other infections include:

| | | |
|---|---|---|
| C-difficile | - | 5 |
| Cellulitis | - | 8 |
| Tracheobronchitis | - | 1 |
| Phlebitis | - | 2 |
| Upper Respiratory | - | 2 |

**Table 3: Final Multivariable Logistic Regression Model for Post-operative Nosocomial Infection**

| Parameter | Odds Ratio | Lower 95% Confidence Limit for Odds Ratio | Upper 95% Confidence Limit for Odds Ratio | p-value |
|---|---|---|---|---|
| Allogeneic Blood | 1.734 | 1.046 | 2.875 | 0.0330 |
| Cardiac Surgery | 4.669 | 2.719 | 8.017 | <0.0001 |
| Age (years) | 1.024 | 1.002 | 1.047 | 0.0332 |
| Renal Disease | 2.479 | 1.268 | 4.847 | 0.0080 |
| Hosmer-Lemeshow Goodness-of-Fit Test p-value = 0.1571 | | Area Under ROC Curve = 0.772 | | |

**Figure 3: Final Logistic Regression Model of Postoperative Infection versus Age by Surgery Type and Blood Management Technique**




## CONCLUSIONS

- Allogeneic blood management was shown to significantly increase the risk of postoperative infections.
- Other factors identified that significantly influence the risk of infection were surgery type, patient age, and renal disease.
- Cardiac surgery and advancing age were associated with a higher probability of postoperative infection. Renal disease may be a surrogate for baseline hemoglobin or hematocrit.

## BLOOD MANAGEMENT DEMONSTRATION GROUP

[1] Aryeh Shander, M.D., Englewood Hospital and Medical Center, Englewood, NJ, [2] David Adams, M.D., University of Vermont, Burlington, VT, [3] Jim Rathmell, M.D., University of Vermont, Burlington, VT, [4] Linda Shore-Lesserson, M.D., Mt. Sinai School of Medicine, New York, NY, [5] Jeff Silverstein, M.D., Mt. Sinai School of Medicine, New York, NY, [6] Robert Bartlett, M.D., Palmetto Health, Columbia, SC, [7] Michael O'Connor, M.D., University of Chicago, Chicago, IL, [8] Kathleen McNicholas, M.D., Christiana Care Health Services, Newark, DE [9] Richard Spence, M.D., Baptist Health System, Burmingham, AL, [10] Ched Singleton, M.D., Baptist Health System, Burmingham, AL, [11] Nader D. Nader, M.D., Veterans Administration Medical Center, Buffalo, NY, [12] Cynthia Walawander, M.A., Cognigen Corporation, Buffalo, NY

## ACKNOWLEDGEMENTS

Betty Johnson, Deborah Smoak, Sherri Ozawa, Phelicia Hobson, Cio DelaRiva, Sarah Ballard, Michael Pietrowicz, Edna Cadmus, Spring Maleckar, Laura Holley, Colette Bradford, Wanda Winfrey, Michele Mitchell-Bligen, Angela DiSabatino, Karen Davis, Paige Larson, Mark Hoeft, Richard Skomra, Cindy Cook, Nancy Cox, Cate Woolston, Leona Lackie, Lisa Amendola, Vivian Masterman, Linda Brokob, Meg Wilber, Pei Lui, Julie Passerell, Beth Ludwig, Phil Vecchione, Karen Nykiel, Junko Kanamura, Colleen Dracup, Patricia Mariani.

*This study was funded by Englewood Hospital and Medical Center, Englewood, N.J.*