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Variability in Transfusion Practice for Coronary Artery Bypass Surgery Persists Despite National Consensus Guidelines

A 24-Institution Study

E. Price Stover, M.D., Lawrence C. Siegel, M.D.,† Reg Parks, M.P.H.,‡ Jack Levin, M.D.,§*
*Simon C. Body, M.B., Ch.B., F.A.N.Z.C.A.,‖ Rosemarie Maddi, M.D.,# Michael N. D'Ambra, M.D.,***
Dennis T. Mangano, Ph.D., M.D.,†† Bruce D. Spiess, M.D.,‡‡
the Institutions of the Multicenter Study of Perioperative Ischemia Research Group

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* Assistant Professor of Anesthesia, Department of Anesthesia, Stanford University School of Medicine.

† Associate Professor of Anesthesia, Department of Anesthesia, Stanford University School of Medicine.

‡ Epidemiologist, Ischemia Research and Education Foundation.

§ Professor of Laboratory Medicine, Department of Laboratory Medicine, University of California, San Francisco.

‖ Instructor in Anesthesia, Department of Anesthesia, Brigham and Women's Hospital.

Assistant Professor of Anesthesia, Department of Anesthesia, Brigham and Women's Hospital.

** Associate Professor of Anesthesia, Department of Anesthesia, Massachusetts General Hospital.

†† Professor of Anesthesia, Department of Anesthesia, University of California, San Francisco.

‡‡ Associate Professor of Anesthesia, Department of Anesthesia, University of Washington, School of Medicine.

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For a complete list of members of the research groups, see Appendices 1 and 2.

Address reprint requests to Dr. Stover: Department of Anesthesia, Stanford University School of Medicine, Stanford, California 94305. Address electronic mail to: stover@leland.stanford.edu

Background: **An estimated 20% of allogeneic blood transfusions in the United States are associated with cardiac surgery. National consensus guidelines for allogeneic transfusion associated with coronary artery bypass graft (CABG) surgery have existed since the mid- to late 1980s. The appropriateness and uniformity of institutional transfusion practice was questioned in 1991. An assessment of current transfusion practice patterns was warranted.**

Methods: **The Multicenter Study of Perioperative Ischemia database consists of comprehensive information on the course of surgery in 2,417 randomly selected patients undergoing CABG surgery at 24 institutions. A subset of 713 patients expected to be at low risk for transfusion was examined. Allogeneic transfusion was evaluated across institutions. Institution as an independent risk factor for allogeneic transfusion was determined in a multivariable model.**

Results: **Significant variability in institutional transfusion practice was observed for allogeneic packed red blood cells (PRBCs) (27–92% of patients transfused) and hemostatic blood components (platelets, 0–36%; fresh frozen plasma, 0–36%; cryoprecipitate, 0–17% of patients transfused). For patients at institutions with liberal rather than conservative transfusion practice, the odds ratio for transfusion of PRBCs was 6.5 (95% confidence interval [CI], 3.8–10.8) and for hemostatic blood components it was 2 (95% CI, 1.2–3.4). Institution was an independent determinant of transfusion risk associated with CABG surgery.**

Conclusions: **Institutions continue to vary significantly in their transfusion practices for CABG surgery. A more rational and conservative approach to transfusion practice at the institutional level is warranted. (Key words: Blood conservation; cardiac surgery; cryoprecipitate; fresh frozen plasma; hemostatic blood components; packed erythrocytes; packed red blood cells; platelets.)**

IT has been estimated that nearly 20% of blood transfusions in the United States are associated with cardiac surgery.[1] National consensus guidelines for the transfusion of allogeneic blood products associated with coronary artery bypass graft (CABG) surgery have existed since the mid to late 1980s.[2–5] However, as late as 1991,

Goodnough *et al.*[6] documented the marked variability in institutional transfusion practice associated with primary (first time operation) CABG surgery. Given a growing public concern for the safety, cost, and adequacy of the national blood supply, as well as increasing pressure to decrease the use of allogeneic blood products,[7] an assessment of current transfusion practice patterns was indicated.

The present multicenter study assessed current perioperative transfusion practices for primary CABG surgery at 24 academic institutions. This evaluation was performed on a carefully selected subset of patients at low risk for transfusion, for whom the greatest uniformity of practice would be expected.

Methods

The Multicenter Study of Perioperative Ischemia (McSPI) database (Epi I) is composed of data from 2,417 patients who underwent CABG surgery with or without concurrent cardiac surgical procedures. With appropriate institutional review board approval and informed patient consent, each of 24 academic institutions studied 100–108 randomly selected patients during a 2-yr period between September 1991 and September 1993. Perioperative data were prospectively recorded by anesthesiologists at each site using a standardized form. Trained investigators at each center collected the data on demographics, procedures, medications, laboratory values, hemodynamic events, support methods (including transfusion therapy), cardiac and noncardiac events, patient transfer, and discharge from medical records. Site and patient identities were blinded to all but key persons at the central analysis unit. All data entry, validation, and statistical analyses were performed using SAS software (SAS version 6.0.9; SAS Institute, Cary, NC).

The effect of a disproportionate distribution of patients at high risk for transfusion among institutions was minimized by selecting a subset of 713 patients, determined by both preliminary analyses (univariate analysis for categorical predictive variables and linear regression analysis for continuous predictive variables) and established literature[8,9] to be at relatively low risk for transfusion therapy. Specifically, patients included in the analysis had elective admission and surgery (*i.e.*, appeared on final operating room schedule, nonurgent, or nonemergent operation), first-time sternotomy and CABG surgery only, were aged less than 75 yr, approximated preoperative erythrocyte volume >1,400 ml, normal preoperative coagulation profile, no perioperative mechanical ventricular assistance, and no reoperation for hemorrhage or death.

Preoperative erythrocyte volume was calculated as weight in kg × 70 ml/kg × preoperative hematocrit (with 65 ml/kg weight used for women). Calculation of estimated erythrocyte volume lost was as follows: [(weight in kg × 70 ml/kg) × (preoperative hematocrit − discharge hematocrit)] + number of allogeneic blood units transfused × 200 ml/unit + number of autologous blood units × 177 ml/unit (with 65 ml/kg weight used for women).[6] Predictor variables included age, preoperative hematocrit, preoperative erythrocyte volume, duration of cardiopulmonary bypass (CPB), and calculated perioperative erythrocyte volume lost. Outcome variables examined included the number and frequency of perioperative transfusions of allogeneic packed red blood cells (PRBCs), platelets, fresh frozen plasma (FFP), and cryoprecipitate. The association between the use of blood conservation techniques (preoperative donation of autologous whole blood, intraoperative erythrocyte salvage, intraoperative normovolemic hemodilution, postoperative reinfusion of shed mediastinal blood) and the transfusion of allogeneic blood products was also examined.

Descriptive analysis of the transfusion data included mean, standard deviation, median, quartile and range values, and percentage of patients transfused with a specific product at each institution. Nonparametric statistical analyses of the transfusion data included likelihood ratio chi-square analysis (for the percentage of patients receiving a particular blood product across institutions), median score, and Kruskal-Wallis tests (for the number of allogeneic PRBC transfusions across institutions). The relation between outcome and predictor variables was examined using Pearson and Spearman correlation coefficients; multiple logistic regression and general linear models were used for multivariable analyses. Stepwise logistic multivariable models for the transfusion of allogeneic PRBCs and hemostatic blood components included the following covariates: age, preoperative hematocrit, estimated preoperative erythrocyte volume, duration of CPB, calculated perioperative erythrocyte volume lost, and a site variable consisting of three groups of institutions defined by their pattern of transfusion frequency (high or low) in response to variable blood loss (high or low).

Results

Figure 1 shows the distribution of patients considered to be at low risk for transfusion across institutions. Four

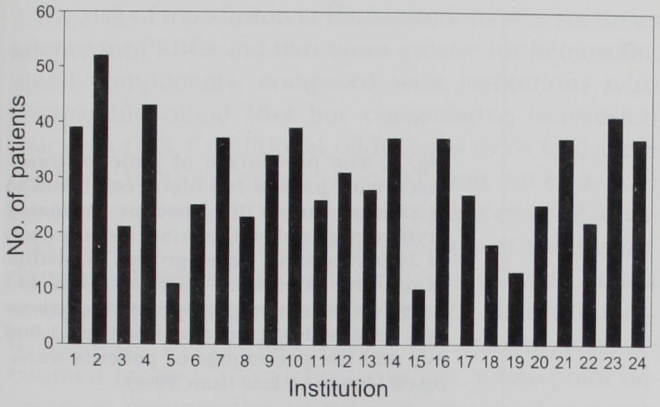

Fig. 1. The number of patients having coronary artery bypass who were at low risk for transfusion at each of the 24 participating institutions from September 1991 to September 1993.

of 24 institutions had fewer than 20 patients who satisfied the criteria for low risk for transfusion, and 10 institutions had 35 or more patients. These 713 low-risk patients constitute the subgroup for all subsequent analyses.

Figure 2A shows the median number of units of PRBCs transfused per patient at each institution. Across institutions, the median number of PRBC units transfused per patient ranged from 0–4 ($P < 0.01$ for variability among institutions). At 13 institutions, ≥50% of patients received no PRBCs. Of the remaining 11 institutions, 9 transfused ≥50% of their patients with 2 or more units of PRBCs, including two centers whose median values were 2.5 and 4 units of PRBCs per patient.

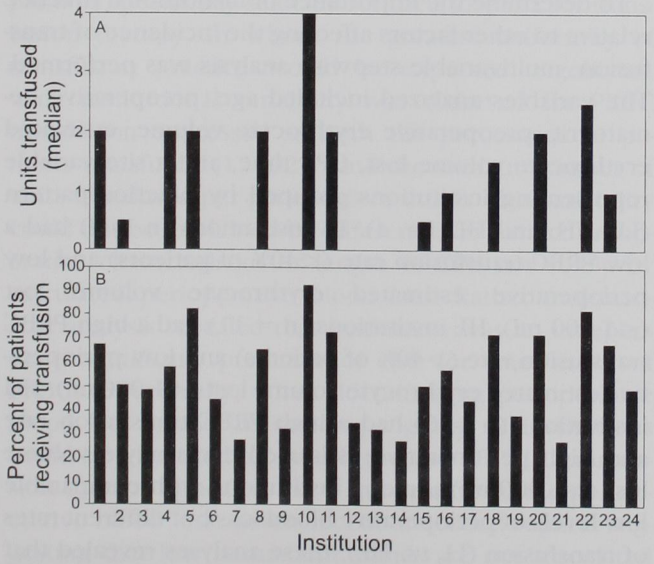

Fig. 2. Packed red blood cell (PRBC) transfusion at 24 institutions. (*A*) The median number of PRBC units transfused per patient is shown for each institution. (*B*) The percentage of patients transfused with PRBCs is depicted for each institution.

The percentage of patients receiving PRBCs at a given institution varied widely from 27% to 92% ($P < 0.01$, fig. 2B). The median value for the percentage of patients among the 24 institutions was 50%. Five institutions transfused <35% of patients with PRBCs, whereas nine institutions transfused PRBCs to >60% of patients.

Figure 3 depicts the institutional practice patterns for hemostatic blood component administration. The percentage of patients receiving platelets at each institution ranged from 0–36% (median, 9%; $P < 0.01$ for variability among institutions; fig. 3A). Four institutions transfused no platelets, and 8 of 24 institutions transfused ≤5% of patients with platelets. In contrast, six institutions administered platelets to >20% of their low-risk patients, with two of these to ≥35% of patients.

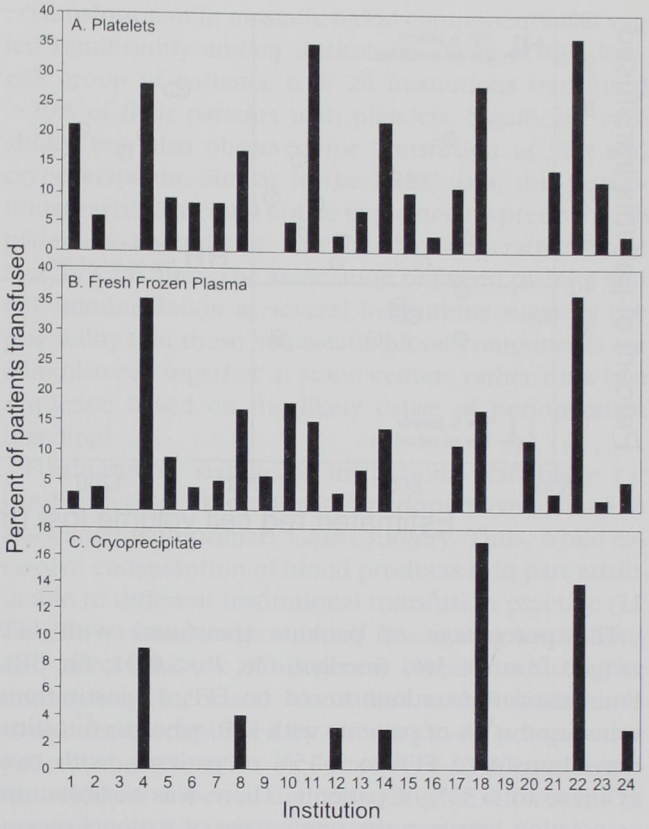

Fig. 3. Hemostatic blood component transfusion at 24 institutions. The percentage of patients transfused with platelets (*A*), fresh frozen plasma (*B*), and cryoprecipitate (*C*) is shown for each institution.

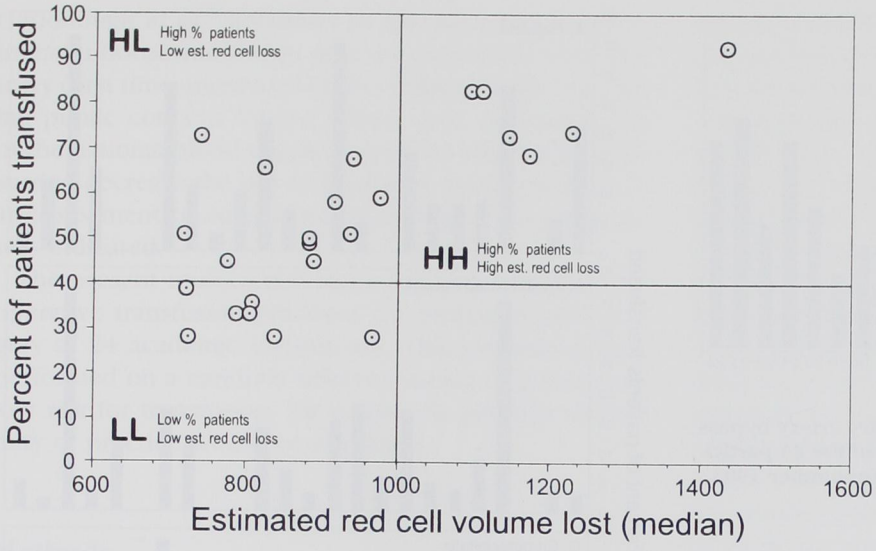

Fig. 4. The percentage of patients transfused with packed red blood cell (PRBCs) is plotted *versus* the median estimated erythrocyte (red cell) volume lost for each of 24 institutions. Three groups of institutions were identified (HH, HL, and LL) based on estimated perioperative erythrocyte volume lost (more or less than 1,000 ml) and the percentage of patients transfused (more or less than 40%).

The percentage of patients transfused with FFP ranged from 0–36% (median, 6%; $P < 0.01$; fig. 3B). Four institutions administered no FFP, 12 institutions transfused ≤5% of patients with FFP, whereas 6 institutions transfused FFP to >15% of patients, with two of these to >35% of patients. There was a substantial association between the percentage of patients receiving platelets and the percentage of patients receiving FFP at a given institution (correlation coefficient [r]; $r^2 = 0.5$). This represented the only strong correlation between institutional transfusion of any pair of allogeneic blood products.

The percentage of patients transfused with cryoprecipitate ranged from 0–17% (median, 0%; $P < 0.02$; fig. 3C). Seventeen institutions transfused no cryoprecipitate. Of the remaining seven centers, two administered cryoprecipitate to >10% of their low-risk patients.

To understand the observed variability in transfusion practice, several factors were examined. The typical predictors of transfusion risk, specifically the median institutional values for age, preoperative hematocrit, preoperative erythrocyte volume, and length of CPB correlated poorly with the institutional risk for PRBC transfusion ($r^2 < 0.16$) or hemostatic blood component transfusion ($r^2 < 0.1$). Only median institutional estimated erythrocyte volume lost correlated substantially with PRBC transfusion, accounting for approximately one half of the variability of erythrocyte transfusions among institutions ($r^2 = 0.52$, fig. 4). For equivalent estimated perioperative erythrocyte volume lost (<1,000 ml), seven institutions transfused <40% of patients with PRBCs, whereas 11 institutions transfused >40% of patients with PRBCs. The variability in estimated perioperative erythrocyte volume lost among institutions was also significant (range, 725–1,450 ml; $P < 0.01$) and could not be explained by institutional differences in preoperative patient characteristics or duration of CPB. The frequency of institutional use of any particular blood conservation technique in this low-risk subset of patients did not correlate ($r^2 < 0.1$) with reduced exposure to allogeneic PRBCs or hemostatic blood components.

To determine the importance of institutional practice relative to other factors affecting the incidence of transfusion, multivariable stepwise analysis was performed. The variables analyzed included age, preoperative hematocrit, preoperative erythrocyte volume, estimated erythrocyte volume lost, CPB time, and a site variable representing institutions grouped by practice pattern (LL, HH, and HL; fig. 4). LL institutions (n = 7) had a low PRBC transfusion rate (<40% of patients) and low perioperative estimated erythrocyte volume lost (<1,000 ml). HL institutions (n = 11) had a high PRBC transfusion rate (>40% of patients) and low perioperative estimated erythrocyte volume lost (<1,000 ml). HH institutions (n = 6) had a high PRBC transfusion rate and high perioperative estimated erythrocyte volume lost (>1,000 ml). Among institutions with comparable low levels of perioperative blood loss but different rates of transfusion (LL *vs.* HL), these analyses revealed that institution was a significant independent predictor of transfusion risk both for allogeneic PRBCs ($P < 0.01$) and hemostatic blood components ($P < 0.02$).

The risk of transfusion at HL institutions was six times greater for PRBCs and two times greater for hemostatic blood components, compared with institutions with comparable blood loss but conservative transfusion practices (LL). Conditional odds ratios (95% CIs) were 6.5 (3.8–10.8) for PRBCs ($P < .01$) and 2.0 (1.2–3.4) for hemostatic blood components (platelets, FFP, cryoprecipitate; $P < 0.02$). The magnitude of the institutional effect (logistic β coefficient) was 0.75 unit PRBCs more per patient at HL compared with LL institutions. In contrast, <0.20 unit PRBCs per patient was accounted for by a 10-yr increase in age, a two-point decrease in preoperative hematocrit expressed as a percentage, a 200-ml decrease in calculated preoperative erythrocyte volume, or a 70-ml estimated perioperative erythrocyte volume lost (200 ml estimated blood loss based on average preoperative and postoperative hematocrit concentrations of 35%). Duration of CPB had no significant effect on the magnitude of PRBC transfusion.

Discussion

Despite published national guidelines[2–5] and previous concern about nonuniform institutional transfusion practices for CABG surgery,[6] the present multicenter study shows that perioperative transfusion practice still varies substantially among academic institutions. This variability was demonstrated among a cohort of 713 patients specifically selected for their low risk for transfusion therapy, in whom the greatest uniformity of transfusion practice would be expected. Significant wide institutional variability was observed for PRBC transfusion expressed as both the percentage of patients transfused (17–92%) and the median number of units transfused per patient (0–4 units). This variability could not be explained by differences in patient preoperative characteristics or length of CPB nor solely by calculated perioperative blood loss. Rather multivariable analysis revealed that institution was an independent, significant predictor of risk for transfusion of PRBCs. Specifically, when documenting perioperative blood loss at the institutions, a group of institutions could be identified for which the use of PRBC transfusion therapy appeared excessive relative to the perioperative blood loss. Given recent anecdotal reports suggesting that low hematocrit values are not associated with increased morbidity,[10,11] and no evidence that higher hematocrit values are associated with decreased morbidity, this practice appears inappropriate.

Transfusion of hemostatic blood components also varied significantly among institutions. Even in this low-risk group of patients, 6 of 24 institutions transfused >20% of their patients with platelets. Significant variability was also observed for transfusion of FFP and cryoprecipitate. Similar to the PRBC data, this institutional variability could not be explained by preoperative patient characteristics, calculated perioperative blood loss, or CPB time. The association between platelet and FFP administration at several institutions suggests the possibility that these hemostatic blood components are administered together at some centers rather than in a sequence based on the likely cause of perioperative bleeding.

Furthermore, significant institutional variability existed with respect to estimated perioperative blood loss associated with primary CABG surgery. Thus, while excessive consumption of blood products is in part attributable to different institutional transfusion practice (LL *vs.* HL), variable surgical blood loss among institutions also affects the use of allogeneic blood products. The finding that increased blood loss at HH institutions could not be explained by differences in preoperative patient characteristics or duration of CPB emphasizes the need for a better understanding of differences in surgical practice pertaining to hemostasis.

Transfusion data from the present investigation are consistent with the enormous range in both the frequency and number of units of PRBCs, platelets, FFP, and cryoprecipitate administered to patients having CABG surgery, as reported in the survey of 740 US hospitals conducted by the College of American Pathologists in 1992.[12] Similarly, in a European multinational study, wide interhospital variations in both the frequency of transfusion and the number of allogeneic units transfused were found.[13]

Previous work by Goodnough *et al.*[6] examined transfusion practice among 30 consecutive patients having primary CABG at each of 18 centers. They also found significant variability in institutional transfusion practice for PRBCs, platelets, and FFP, and they further showed that institution independently influenced transfusion of PRBCs. The present study selected a more homogeneous and relatively lower risk (for transfusion) study population than did Goodnough *et al.*[6] In addition, institutions were grouped by transfusion practice in response to variable blood loss to quantify the independent effect of site. The present finding that significant variability persists for transfusion of PRBCs and hemostatic blood components, even in a low-risk popu-

lation, is therefore disturbing. So too is the current finding that institution is an independent predictor of transfusion risk for both PRBCs and hemostatic blood components. It is remarkable that simply having surgery at an institution with liberal transfusion practice (HL) results in an increased transfusion exposure of 0.75 unit of PRBCs per patient.

Limitations of the present study include the observation that 4 of the 24 institutions had <20 patients who satisfied the low-risk criteria. However, to determine the significance of the observed variability in transfusion practice among institutions, statistical analyses, particularly the Kruskal-Wallis test and likelihood ratio Chi-square, were used that specifically accounted for the few institutions with small numbers of patients. Even when all four institutions with <20 patients were excluded from analysis, significant institutional variability was still present for both PRBCs and hemostatic blood components. Further, the removal of HH institutions from the multivariable analysis reported here minimized the contribution of institutions with excessive blood loss and excessive transfusions. It was also recognized that potential risk factors for transfusion might have been disproportionately distributed across institutions, thus contributing to any observed variability. The use of a carefully defined subset of patients at low risk for transfusion minimized the effect of risk factors other than institution on variability. It is unfortunate that the institutional use of antifibrinolytic therapy was not tracked in this database. In addition, the use of any particular blood conservation technique did not correlate with decreased transfusion rate in this low-risk subset of patients. Thus any differences in blood conservation practice probably exerted little influence on the observed variability in transfusion behavior among institutions. Finally, changes in personnel and thus individual practice patterns at a given institution over the relatively long data collection period (2 yr) could have influenced variability, but all institutions should have been at relatively equivalent risk for small changes in practitioners.

In conclusion, the present data clearly show that inappropriate transfusion practice continues at a significant proportion of leading academic institutions. A more rational approach to transfusion practice at the institutional level is clearly warranted, especially given the significant costs and hazards associated with transfusion therapy.[14] At many centers, cardiac surgery accounts for a substantial portion of the total institutional use of allogeneic blood components. Recent multicenter quality assurance efforts have been associated with a reduction in perioperative transfusions in cardiac surgery.[15] At a minimum, clinicians must be cognizant of established national guidelines and should match their institutional transfusion practices to those of institutions using appropriate transfusion therapy with comparable outcomes. To achieve this important goal, institutional examination of a well-defined subpopulation of patients at low risk for transfusion, as described in the present study, may allow for more ready identification of systematic problems in transfusion practice.

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Appendix 1

McSPI Analysis Group

Director: Dennis T. Mangano, Ph.D., M.D.

Data Management/Statistical Analysis: Reg Parks, M.P.H.; Long Ngo, M.S.; Elizabeth Li, M.S.

Clinical Consultant: Gerard M. Ozanne, M.D.

Electrocardiographic Analysis: Milton Hollenberg, M.D.; Krzystof Ziola, M.D.; Mervin Goldman, M.D.; Adrianna Radulescu, M.D.

Cardio/Cerebrovascular Outcome Validation: Dennis T. Mangano, Ph.D., M.D.; Uday Jain, Ph.D., M.D.; Milton Hollenberg, M.D.; Steven Graham, M.D., Ph.D.

Editorial Assistants: Winnifred von Ehrenburg, Diane Beatty, Mark Riddle

Appendix 2

Participating McSPI Investigators and Institutions

Anil Aggarwal, M.D., VA Medical Center, Milwaukee, WI

Wayne H. Bellows, M.D., Kaiser-Permanente Medical Center, San Francisco, CA

Gary Roach, M.D., Kaiser-Permanente Medical Center, San Francisco, CA

Simon Body, M.D., Brigham and Women's Hospital, Boston, MA

Rosemarie Maddi, M.D., Brigham and Women's Hospital, Boston, MA

Randall Clark, M.D., Baylor College of Medicine, Houston, TX

Patrick E. Cluring, MD Baylor College of Medicine, Houston, TX

Salwa Shenaq, M.D., Baylor College of Medicine, Houston, TX

Mark E. Comunale, M.D., Beth Israel Hospital, Boston, MA

Michael N. D'Ambra, M.D., Massachusetts General Hospital, Boston, MA

Judith Fabian, M.D., Medical College of Virginia, Richmond, VA

Richard Wolman, M.D., Medical College of Virginia, Richmond, VA

Richard Fine, M.D., Cornell University Medical Center, New York, NY

Onofrio Patafio, M.D., Cornell University Medical Center, New York, NY

Arnold S. Friedman, M.D., Cedars-Sinai Medical Center, Los Angeles, CA

Mark Goldstein, M.D., Texas Heart Institute, Houston, TX

Stephen Slogoff, M.D., Texas Heart Institute, Houston, TX

Marc Kanchuger, M.D., New York University Medical Center, New York, NY

Katherine E. Marschall, M.D., New York University Medical Center, New York, NY

Colleen Koch, M.D., The Cleveland Clinic Foundation, Cleveland, OH

Norman J. Starr, M.D., The Cleveland Clinic Foundation, Cleveland, OH

William Leil, M.D., University of Alabama at Birmingham, Birmingham, AL

Joseph P. Matthew, M.D., Yale University School of Medicine, New Haven, CT

Christina Mora, M.D., Emory University Hospital, Atlanta, GA

James G. Ramsay, M.D., Emory University Hospital, Atlanta, GA

Thomas E. Stanley, M.D., Duke University Medical Center, Durham, NC

Gerard M. Ozanne, M.D., VA Medical Center, San Francisco, CA

Allan F. Ross, M.D., University of Iowa, Iowa City, IA

Winnie Ruo, M.D., University of Chicago, Chicago, IL

Mark Trankina, M.D., University of Chicago, Chicago, IL

Joseph S. Savino, M.D., University of Pennsylvania, Philadelphia, PA

Bruce Spiess, M.D., University of Washington, Seattle, WA

Lawrence C. Siegel, M.D., Stanford University Medical Center, Stanford, CA

E. Price Stover, M.D., Stanford University Medical Center, Stanford, CA

Kenneth J. Tuman, M.D., Rush Presbyterian, St. Luke's Medical Center, Chicago, IL

Joyce Wahr, M.D., University of Michigan, Ann Arbor, MI