EDITORIAL

Patient blood management during cardiac surgery: Do we have enough evidence for clinical practice?

Marco Ranucci, MD,[a] Solomon Aronson, MD,[b] Wulf Dietrich, MD, PhD,[c] Cornelius M. Dyke, MD,[d] Axel Hofmann, ME,[e,f] Keyvan Karkouti, MD,[g] Marcel Levi, MD, PhD,[h] Gavin J. Murphy, MD, FRCS,[i] Frank W. Sellke, MD,[j] Linda Shore-Lesserson, MD,[k] and Christian von Heymann, MD,[l] endorsed by the European Association of Cardiothoracic Anaesthesiologists (EACTA)

Transfusion of allogeneic blood products during and after cardiac operations is common. When the degree of anemia and the consequent decrease in oxygen delivery lead to organ ischemia, there is little doubt that red blood cell (RBC) transfusion is necessary. In addition, treatment with fresh-frozen plasma and platelets may be necessary to support coagulation. Treatment with blood products may also aim to prevent hemodynamic instability from excessive postoperative blood loss. A large body of evidence, however, indicates that transfusion of blood products per se may be associated with increased morbidity and mortality after cardiac operations.[1-4] It is therefore important to assess the real versus perceived need for the transfusion of allogeneic RBCs and other blood products by examining the risk–benefit profile of blood product transfusion relative to the clinical condition of the patient. The risk–benefit profile of blood product transfusion depends on many factors but is primarily based on the hemoglobin value. Other important factors include patient age, sex, hemodynamic profile, and signs of organ dysfunction.[5,6] The risks of infectious disease transmission[1] and immunologic suppression,[7] the costs, and a diminishing blood supply also contribute to the direct risk–benefit decision analysis and the overarching impetus to develop alternatives to blood component transfusion. The decision-making processe that determines whether to transfuse, when to transfuse, which blood products to transfuse, and how much of any product to transfuse are indeed complex and need to include an evaluation of both the risks of transfusion and perioperative anemia and a discussion about blood conservation strategies.

This topic was addressed by a comprehensive document on perioperative blood conservation in cardiac surgery released by the Society of Thoracic Surgeons and the Society of Cardiovascular Anesthesiologists.[8] This document provides guidelines for the use of RBCs, fresh-frozen plasma, and platelets in the setting of a cardiac operation, providing appropriate hemoglobin cutoff values for erythrocyte transfusions, which vary widely depending on the clinical scenario. Although these guidelines address a number of very important issues and are largely followed in the structured context of clinical studies, the recommendations have not been widely accepted in clinical practice, as was recently demonstrated by a survey among anesthesiologists.[9] This lack of acceptance may be attributable to a perceived lack of evidence, a lack of awareness of the guidelines, logistic issues related to the blood supply, institutional dogma, or policies that are based on economic considerations. Any or all of these factors may contribute to a reluctance to change institutional patient blood management.

The concept of patient blood management includes different strategies that aim to avoid unnecessary transfusions. The pillars that contribute to this concept are (1) the optimization of patient RBC mass, (2) the minimization of blood loss, and (3) the optimization of physiologic anemia tolerance. The comprehensive concept of patient blood management may soon replace the more simplistic

From the Department of Cardiothoracic-vascular Anesthesia and Intensive Care,[a] IRCCS Policlinico S. Donato, Milan, Italy; the Department of Anesthesiology,[b] Duke University Medical Center, Durham, NC; the Working Group on Perioperative Hemostasis,[c] Department of Anaesthesia, Ludwig Maximilian University Muenchen, Munich, Germany; SouthEast Texas Cardiovascular Surgery Associates, PA,[d] Houston, Tex; Centre for Population Health Research,[e] Curtin Health Innovation Research Institute (CHIRI), Curtin University, Perth, Western Australia; the Medical Society for Blood Management,[f] Laxenburg, Austria; the Department of Anesthesia,[g] Toronto General Hospital, University Health Network, University of Toronto, Toronto, Ontario, Canada; the Department of Vascular Medicine and Internal Medicine,[h] Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands; the Bristol Heart Institute,[i] University of Bristol, Bristol Royal Infirmary, Bristol, United Kingdom; the Division of Cardiothoracic Surgery,[j] Alpert Medical School of Brown University, Rhode Island Hospital, Providence, RI; the Department of Anesthesiology,[k] Cardiothoracic Anesthesiology, Montefiore Medical Center, Bronx, NY; and the Department of Anaesthesiology and Intensive Care Medicine,[l] Charité-Universitätsmedizin Berlin, Berlin, Germany.

Disclosures: The author group comprises the International Initiative on Haemostasis Management in Cardiac Surgery (IIHMCS). Members of the group were compensated for their presence at face-to-face meetings but not for the time invested in developing and reviewing the manuscript. Meeting organization and medical writing support for literature searches and manuscript preparation were provided by Physicians World Europe GmbH, Mannheim, Germany. Costs incurred for travel, hotel accommodation, meeting facilities, honoraria and preparation of the manuscript were supported by an unrestricted educational grant from Novo Nordisk Health Care AG, Zurich, Switzerland. The sponsor had no authorship or editorial control over the content of the meetings or any subsequent publication.

Drs Marco Ranucci and Solomon Aronson are co–first authors and cochairs of the International Initiative for Haemostasis Management in Cardiac Surgery (IIHMCS).

Received for publication Jan 24, 2011; revisions received Feb 9, 2011; accepted for publication April 8, 2011; available ahead of print May 23, 2011.

Address for reprints: Marco Ranucci, MD, Department of Cardiothoracic-vascular Anesthesia and Intensive Care, IRCCS Policlinico S. Donato, Via Morandi 30, San Donato Milanese, Milan, 20097, Italy (E-mail: cardioanestesia@virgilio.it).

0022-5223/$36.00

doi:10.1016/j.jtcvs.2011.04.007

Abbreviations and Acronyms

ACS = acute coronary syndrome
ACT = activated clotting time
ANH = acute normovolemic hemodilution
CABG = coronary artery bypass grafting
CPB = cardiopulmonary bypass
HES = hydroxyethyl starch
ICER = incremental cost-effectiveness ratio
ICU = intensive care unit
IIHMCS = International Initiative on Haemostasis Management in Cardiac Surgery
mini-CPB = minimal cardiopulmonary bypass
RBC = red blood cell
RCT = randomized, controlled trial
rFVIIa = recombinant activated factor VII
rSo_2 = regional cortical oxygen saturation
$Scvo_2$ = central venous oxygen saturation
Svo_2 = mixed venous oxygen saturation
TRICC = Transfusion Requirements in Critical Care
TTDR = total transfusion dependency ratio

''transfusion containment'' or ''blood conservation'' approaches.

At present, patient management is highly heterogeneous in different countries and institutions, and the recognition that allogeneic blood products may do harm does not seem to be widespread. A recent survey of nearly 25,000 patients undergoing coronary artery bypass grafting (CABG) in US institutions followed up from hospital admission until 30 days after discharge found large interinstitutional differences, accounting for 30% of the variance in transfusion practices. Allogeneic blood use ranged from 50% to 100% among patients at different institutions, and 78.5% of the male and 93.6% of the female patients received allogeneic blood products during the hospital stay, implying that many of these transfusions may have been unnecessary.[10] Similarly, a clinical trial comparing functional outcome after administration of a liberal versus restrictive transfusion regimen showed no benefit for the liberal transfusion group.[11]

The authors of this article comprise the International Initiative on Haemostasis Management in Cardiac Surgery (IIHMCS). We believe that many of the factors that influence the decisions and behavior surrounding transfusion of allogeneic blood products are not adequately addressed by the existing literature. One reason for this may be the lack of information available within existing databases used to determine the risk of transfusion during and after cardiac operations. Whereas traditional guideline and consensus papers review the weight of evidence to establish a rationalization for a position or plan of action, we have here sought to evaluate the evidence that exists to establish a ''call to action'' to fill the gaps and define the needs for further evidence.

The aims of this article are as follows: (1) to assess the level of evidence for indications and risk factors associated with transfusion of allogeneic RBCs and other blood products, (2) to identify evidence gaps and prioritize the evidence gaps with respect to potential impact on modifying practice and outcomes, and (3) to recommend possible actions to fill the evidence gaps, including but not limited to defining perioperative factors that should in future be included in existing databases.

MATERIALS AND METHODS

Comprehensive computer database literature searches were performed with the indexed online database MEDLINE/PubMed. Lists of cited literature within relevant articles and our own libraries were also screened. The primary intention of the review was to identify prospective randomized, controlled trials (RCTs), existing systematic reviews, and current guidelines. Boolean operators and Medical Subject Heading thesaurus keywords were applied as a standardized use of language to unify differences in terminology into single concepts. The scientific questions posed and the Medical Subject Heading headings applied to each search are listed in Appendix Table 1. Searches were limited to English-language abstracts and human studies, all in adults at least 19 years old, and the time period was limited to between January 1994 and April 2009. Full publications were retrieved on the basis of evaluated abstracts that were deemed relevant to the queries posed.

This author group comprises an international, multidisciplinary medical collaboration, the International Initiative on Haemostasis Management in Cardiac Surgery (IIHMCS), with both interest and expertise in the perioperative management of bleeding associated with cardiac surgery blood conservation and transfusion avoidance. The IIHMCS group includes members with specialties in cardiac surgery, cardiac anesthesia, hematology, and medical economics. As IIHMCS authors, we performed the selection of the scientific inquiries to be addressed, the screening and review of the literature to be included, the formulation of a summary of each section, and the complete manuscript review. The group participated in 2 face-to-face meetings in February and October 2009 and a web conference in July 2009 as part of the manuscript development process. The IIHMCS group was managed by Physicians World Europe GmbH, Mannheim, Germany, and its activities were supported by an unrestricted educational grant from Novo Nordisk Health Care AG, Zurich, Switzerland.

RESULTS AND DISCUSSION

Physiologic Signs of Organ Dysoxia

Adequate organ oxygenation is fundamental for physiologic organ function. Normally, the amount of oxygen delivered to the whole body exceeds resting oxygen requirements by several fold.[12] Tissue hypoxia occurs if oxygen delivery, defined as the product of arterial oxygen content and cardiac output, decreases to a level at which it is no longer adequate to meet the metabolic demands of the organs. Because hemoglobin-bound oxygen represents a major fraction of arterial oxygen content, increasing hemoglobin levels by RBC transfusion appears to be a logical