Response to Letter “Going beyond Manufacturers’ Limitations Is Not in the Best Interests of Our Patients” by Gerard J. Myers

To the Editor,

We appreciate Mr. Myers’ letter because it adds to the discussion of our article and is interesting. We respect his personal concerns regarding the publication.

Our article is not the first retrospective study to associate lower priming volumes with higher nadir hemoglobin levels and less allogeneic blood use. We cited and discussed those references in the article (1). It is true, in any institution, “excessive hemodilution can be a manageable risk factor if addressed by reliable staff education, common sense, team work and the cooperation of all professions involved in cardiac surgery.”

Regarding internal validity, multiple variables, and the weaknesses of retrospective studies, Mr. Myers restates in his letter what we admonished in the article. As months went by, our team was able to safely select the use of smaller circuits in a greater percentage of our patient population. In addition to the small significant increase in nadir hemoglobin, we reported a significant reduction in the percent of patients receiving allogeneic red blood cells. We also reported a significant reduction in median red blood cell use and direct costs in specific morphology patient subgroups.

Mr. Myers writes that it is common practice to use oxygenators outside of the manufacturer’s reported rated blood flow limits. His letter warns that there are ethical and federal regulatory issues associated with off-label use of medical devices. Is selecting an oxygenator with a maximum flow rate that more closely approximates a patient’s blood flow needs “off-label use” of a device? Modifying cardiopulmonary bypass circuits to reduce hemodilution was classified as a Class I Level of Evidence A recommendation in the guidelines published in 2006 (2). Manufacturers test oxygenators at normothermia with high hemoglobin levels, high blood flow rates, and low mixed venous hemoglobin oxygen saturations that are much more challenging to the device than the normal clinical values experienced during cardiopulmonary bypass. Regarding Mr. Myers’ statement “…the authors would push a small adult oxygenator, the RX15, beyond its manufacturer maximum rated flow of 5 L/min,” in reality, the RX/FX15 oxygenator was tested to an American Association for Medical Instrumentation standard of 7.0 LPM according to the manufacturer’s published instructions for use and specifications. Furthermore, blood flow calculations based on body surface area frequently overestimate flow requirements, particularly in patients with high body mass index (3,4).

Mr. Myers is an expert regarding gaseous microemboli behavior during cardiopulmonary bypass. His points about gaseous microemboli (GME) are difficult to argue, especially when using pediatric devices outside the rated blood flow limits as he cites. The W30 reservoir received its 4.0 LPM flow rating because it was associated with a prior SX oxygenator model and was not separately tested with the RX15 reservoir. Interestingly, the association with the SX model and its maximum flow of 4.0 LPM was before the use of vacuum-assisted venous drainage. The perfusion community uses a 3/8-inch venous line for flows up to 5.0 LPM without vacuum. Therefore, why would such a limitation be placed on the W30 reservoir? The oxygenators are the same. If a RX 15 oxygenator is placed with a W30 reservoir or a W40 oxygenator, it is still an opportunity to provide flow up to 7 L/min. Perfusionists using devices outside the manufacturer limits should study and understand the consequences for the patient in their own clinical setting, including GME creation and removal patterns.

Using our device selection chart, each perfusionist had the liberty to tailor their circuits to the patient needs including arteriovenous (A-V) loop reductions and oxygenator/reservoir size selection. The goal behind creating the chart was to guide our teammates to consistently select the ideal minimum-sized oxygenator/reservoir/A-V loop combination to provide a circuit designed specifically based on the patient’s expected needs. These are steps toward standardization.

Ethically, a perfusionist should hold the patient’s best interests first and foremost. Albeit a small decrease in dynamic priming volume, the RX15 oxygenator it is still 115 mL less prime than the RX25 oxygenator. Add to that a decrease in all other components of our circuit that we improved, and you will find that the result is clinically significant, as reported in our experience. The recently updated AmSECT Standards and Guidelines for Perfusion Practice Standard 9 emphatically states perfusionists should expend efforts to minimize hemodilution, avoid unnecessary blood transfusions, and minimize the bypass circuit size (5).

The practice of perfusion has changed through the years in part because instructions for use (IFUs) are not held as
Iron-cast. Manufacturer IFUs are not just designed to direct safe medical practice but to protect the integrity of the product and the liability of the manufacturer. Off-label use of drugs and medical devices should be respected but not feared by perfusionists, because the practice is openly permitted through relevance to Continuing Medical Education (CME). According to The National Task Force on CME Provider/Industry Collaboration, the off-label use of medical devices is quite common and “...the patterns of off-label use are quite variable, with a range from single digits to up to 80% of use...” (6).

“A presentation of an off-label indication within the context of a continuing medical education activity is intended to provide healthcare providers with the most current clinical evidence for all available treatment options...” The National Task Force indicates that “...a discussion must be evidence-based, should be strictly limited to the discretion of the accredited provider within the activity, and cannot be positioned to encourage or promote off-label use for commercial purposes.”

The article being critiqued does meet these educational goals because it was presented to perfusionist peers in our profession's educational journal, the Journal of Extracorporeal Technology, without promoting commercial gain. The sharing of that practice amidst peers in an educational journal is CME and is acknowledged as common practice.

The word “prescriptive” was used in a high frequency throughout the text because that is exactly what was done. Call it what you will, we are providing a customized circuit to decrease hemodilution, increase nadir hemoglobin, decrease blood transfusions, and decrease associated risks to the patient and costs to everyone.

The benefits of minimizing hemodilution of patients undergoing cardiopulmonary bypass are well proven and simply no longer just a consideration but an ethical obligation for perfusionists. Those willing to make progress and contribute to improvement will always be those taking on a challenge and testing the limits of success.

Operating a medical device outside of a manufacturer’s specification while using it within its designed indication and safely monitoring its performance is not off-label use, but progress.

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REFERENCES