Are We Using the Right Fluid Mechanics Principles?

To the Editor:

We read the article of Yoshida and colleagues [1] with great interest. They showed that patients with severe aortic stenosis are inclined to type IIA von Willebrand factor (vWf) syndrome, which may be reduced by aortic valve replacement. The authors also reported that patients with valvular prosthesis mismatch may not fully benefit from a reduction in vWf abnormalities, because patient-prosthesis mismatch can lead to a residual aortic stenosis. To explain these findings, the authors stated that high shear stresses within the flow jet may cleave vWf multimers. Although the conclusion of this study is relevant, we have concerns with respect to the computations of shear stresses.

The following equation was used by Yoshida and colleagues [1] and by Vincentelli and colleagues [2]: shear stress = (4 × blood viscosity × mean velocity)/(stenosis radius). This equation is not adapted to flow through aortic stenosis. Therefore we believe that some theoretical points must be clarified.

The equation is only valid for a fully developed Hagen-Poiseuille or Womersley (in a time-averaged sense) laminar flow in a circular conduit [3]. This may justify application in the common carotid artery as in the article of Gnasso and colleagues [4]. However, an extrapolation to aortic stenosis is not appropriate, because the corresponding flow characteristics are far different from those in a tube [5].

Assuming that the aforementioned conditions are fulfilled, the equation allows computation of shear stress at the arterial wall only, but not within the flow volume.

In the equation, "mean velocity" refers to spatially averaged velocity, whereas Yoshida and colleagues [1] used the mean temporal velocity.

High shear stresses that would be prone to cleave vWf multimers in aortic stenosis are not located at the level of the vena contracta or along the wall. The jet is indeed lost in a downstream region of turbulent mixing that involves high shear stresses and significant fluid energy dissipation. An estimation of the fluid energy loss may have been more appropriate for global characterization of shear stresses [6].

Although the shear stresses computed in this study are invalid, this does not, however, affect the general conclusions of the authors. A correct application of the fundamentals of fluid mechanics would probably have resulted in higher correlations. Therefore we believe that it is important to be aware of the hypotheses and limitations of fluid mechanics equations and to be watchful when extrapolating the use of such equations.

Lyes Kadem, Eng, PhD
Damien Garcia, Eng, PhD

Laboratory of Biomedical Engineering
Clinical Research Institute of Montreal (IRCM)
110 Pine West Avenue
Montreal, QC, H2W 1R7 Canada
e-mail: lyes.kadem@ircm.qc.ca;
damien.garcia@ircm.qc.ca

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Reply

To the Editor:

We would like to thank Drs Kadem and Garcia [1] for their letter regarding acquired von Willebrand disease with high shear stress aortic valve stenosis [2]. Recently several dynamic in vivo and in vitro studies have shown that anatomic asymmetry of the normal aortic root produces a dynamic deformation. Unfortunately, precise information on time-related changes in flow patterns at the aortic root is lacking (ie, the flow pattern of aortic root changes between rest and exercise). Therefore we used the formula (shear stress = 4 × blood viscocity × mean velocity/stenosis radius) reported by Gnasso and colleagues [3]. This equation is an approximate expression of shear stress at the aortic root, because an accurate equation of shear stress is not yet known.

We had not found the article regarding the energy loss index by Garcia and colleagues [4] when we wrote our article. In their excellent study, Garcia and colleagues [4] recently reported the energy loss index, which has the potential to indicate the severity of energy loss in aortic root downstream from a stenosed aortic valve. If we have an opportunity to report the correlation between patient-prosthesis mismatch and von Willebrand factor in the future, we will use their energy loss index measured by Doppler echocardiography. We thank Drs Kadem and Garcia [1] for their comment.

Kazunori Yoshida, MD
Satoshi Tobe, MD
Masahiro Yamaguchi, MD

Department of Cardiovascular and Thoracic Surgery
Akashi Medical Center
743-33 Okubo-cho Yagi
Akashi, 674-0063, Japan
e-mail: kazu.y-akashi@amc1.jp

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Caution With the Use of Recombinant Activated Factor VII in Treating Postoperative Hemorrhage in Cardiac Surgery

To the Editor:

We congratulate Bishop and colleagues [1] for investigating the use of recombinant factor VIIa (rFVIIa) as a "rescue therapy for uncontrollable postoperative haemorrhage after cardiac surgery," which is a challenging and potentially life-threatening complication. However we would like to raise the following 3 issues:

1. Since the Food and Drug Administration (FDA) first licensed rFVIIa, in 1999 for use in patients with hemophilia, its use has been expanded to include bleeding in nonhemophilia patients, but without a clear consensus on the clinical indications [2]. Furthermore, concerns have been raised about its safety and efficacy in the latter group of patients with several reported cases of thromboembolic adverse events in the literature [2]. These include cerebrovascular accidents, myocardial infarction, peripheral arterial thrombosis, pulmonary embolism, and deep venous thrombosis. There is also evidence in the literature that such adverse events due to "off-label" use of rFVIIa are underreported [2]. A recently published systematic review of literature about pharmacologic uses of rFVIIa identified 28 clinical trials in addition to about 300 case series and reports. It demonstrated that the use of rFVIIa was safe and effective in more than 90% of patients with hemophilia and other coagulation disorders. However the authors stated that there was not enough evidence to support the use of rFVIIa in patients without pre-existing coagulation disorder presenting with severe bleeding with or without surgery [3].
2. The cause and effect relationship is not clear in the study [1]. The pre-rFVIIa coagulation screen was performed between the first cycle and the second cycle of non-red cell blood product support according to the management protocol of the cases reported. However, the post-rFVIIa coagulation screen was performed after both the second cycle of non-red cell blood product support and rFVIIa had been given. It is our contention that before any conclusions can be made about the cause and effect relationship between rFVIIa and the control of postoperative bleeding in this study, there should have been a control group consisting of patients who had been administered a second cycle of non-red cell blood product support, but without rFVIIa for comparison.
3. A particularly important safety concern with the use of rFVIIa in cardiac surgery is the potential for inappropriate clotting [4]. After cardiac surgery with cardiopulmonary bypass, there is upregulation of tissue factor expression both locally in areas of tissue injury as well as systemically [5, 6]. Given that the mechanism of action for rFVIIa involves binding to tissue factor [7], therefore increased tissue factor expression may lead to more systemic clot formation [4]. Furthermore, many cardiac surgery patients have vulnerable atherosclerotic plaques in their coronary vasculature; therefore excessive thrombin generation by rFVIIa may increase the incidence of acute coronary syndromes during the perioperative period [4].

We believe that a degree of caution should be applied regarding the use of rFVIIa in the control of excessive surgical bleeding after cardiac surgery, particularly in absence of both clear guidelines and evidence from clinical randomized trials.

Sharif Al-Ruzzeh, PhD, FRCS
Amr Mahmoud, MS, FCARCSI
Samir Shah, MS, FRCS
David O'Regan, MD, FRCS

The Yorkshire Heart Centre
Leeds General Infirmary
Great George Street
Leeds, LS1 3EX United Kingdom
e-mail: sharifalruzzeh@hotmail.com

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Reply

To the Editor:

My co-authors and I are greatly appreciative of the comments by Al-Ruzzeh and colleagues [1] regarding the use of recombinant activated factor VII (rFVIIa) in the treatment of postoperative hemorrhage in cardiac surgery. As they point out, factor VIIa was used as rescue therapy for uncontrollable postoperative hemorrhage, which is indeed challenging and life threatening. The points they make are appropriate and valid.

1. The use of rFVIIa in our study was entirely off-label [2]. We are indeed concerned about the possibility of intravascular thrombosis, and we were aware of reports in the literature of cerebrovascular accidents, myocardial infarction, and peripheral thrombosis. However, the overall reported rate of major adverse events was approximately 1%, although it is certainly probable that these complications are underreported. However, the reality in the clinical setting we faced was that the patients were bleeding

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