Reply to Schachner

Song Wan*
Division of Cardiothoracic Surgery,
The Chinese University of Hong Kong, Prince of Wales Hospital,
Hong Kong, PR China
Jamie Y. Jeremy
Bristol Heart Institute, University of Bristol, Bristol, UK

Received 31 May 2006; accepted 1 June 2006; Available online 21 July 2006

Keywords: Coronary artery bypass grafting; Fibrin glue; Medial thickness; Neointima; Vein graft

We thank Dr Schachner for his interest and comments on our recent experimental findings [1]. The first facet of our study was that although initially (at 1 month), neointima formation in vein grafts was inhibited by perivenous application of fibrin glue at the time of implantation, at 4 months neointimal formation was not significantly different from controls [1]. Dr Schachner has implied that this is of no consequence. It is a widely held view that neointima formation is axiomatic in promoting vein graft failure [2]. The study therefore demonstrates that there may be a rebound effect that is manifest over the longer term. This also indicates that with acute or pulse treatments of vein grafts with fibrin glue or indeed cytostatic drugs or even gene transfer, care should be exercised when assessing effects at one month only and that potential rebound effects at later time points should be taken into account.

Secondly, Dr Schachner has also suggested that increased medial thickening but no change in luminal area in response to fibrin glue at 4 months could be perceived as a “positive remodeling” effect. We accept that medial thickening is a necessary adaptive response of saphenous vein grafts to arterial conditions and have stated so on many occasions [3,4]. However, excessive thickening of the media may be equally as deleterious as neointima formation. Since medial thickening involves the proliferation of vascular smooth muscle cells and the deposition of matrix proteins, our data at 4 months indicate that these key events are actively occurring in these vein grafts at this time point. Although we did not study effect of fibrin glue in the longer term, it is reasonable to suggest that the trend toward excessive thickening may continue. Indeed, graft thickening in man has long been recognized to become clinically significant at 12–24 months after surgery [2], that is, over more prolonged time courses. Furthermore, vein graft hyperplasia is more aggressive at the anastomoses of vein into artery grafts, sites at which fibrin glue may be applied by surgeons to prevent bleeding. Fibrin glue may be particularly deleterious at these sites by augmenting hyperplasia. Such effects are perhaps not surprising since fibrin is a potent mitogen for vascular smooth muscle cells [5].

Thus, despite the interesting views of Dr Schachner, we reaffirm our conclusions that the application of fibrin glue may elicit untoward effects on vein graft thickening that in the long term may compromise vein graft patency.

References


Letter to the Editor

Systemic oxidative stress associated with lung resection during single lung ventilation

Paul M. Heerdta,b,*
Paul B. Laneb
Mark J. Crabtreeb
Bernard J. Parkc

aDepartment of Anesthesiology, Weill Medical College of Cornell University, Memorial Sloan-Kettering Cancer Center, 525 East 68th Street, Lodon 2, Box 50, New York, NY 10021, United States
bDepartment of Pharmacology, Weill Medical College of Cornell University, 525 East 68th Street, Lodon 2, Box 50, New York, NY 10021, United States

cDepartment of Surgery, Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York, NY 10021, United States

Received 21 April 2006; accepted 29 May 2006; Available online 20 July 2006

Keywords: Oxidative stress; Lobectomy; eNOS; Tetrahydrobiopterin
We read with interest the recent report from Misthos et al. [1] describing the relationship between oxidative stress and cardiopulmonary complications following lung resection. These investigators [2] as well as others [3] have previously linked the intentional collapse and subsequent re-expansion of the operative lung with increased plasma and urinary levels of malondialdehyde (MDA), a stable non-specific marker of lipid peroxidation by free radicals. Of particular note in the recent report was the increased incidence of pulmonary hypertension in patients that had undergone intentional lung collapse for ≥120 min. Although the methods for quantification of changes in pulmonary arterial pressure in this clinical population are not described, the data appear qualitatively consistent with observations we have made during an ongoing study in swine focusing upon specific, physiologically active byproducts of perioperative oxidative/nitrosative stress.

One of the prominent regulators of pulmonary vasomotor tone is nitric oxide (NO) released from endothelial NO synthase (eNOS) following conversion of L-arginine to L-citrulline + NO in the presence of the essential cofactor tetrahydrobiopterin (BH4) [4]. In the setting of both chronic and acute oxidative stress, BH4 bioavailability is diminished largely as a consequence of oxidation to dihydrobiopterin (BH2) [4]. Although both pterin moieties bind to eNOS with similar affinities, BH2-bound eNOS produces superoxide instead of NO. Accordingly, events that elicit pterin oxidation facilitate the formation of subpopulations of NO-producing and superoxide-producing eNOS, ultimately promoting formation of peroxynitrite (ONOO⁻). More reactive than either parent radical, ONOO⁻ can illicit further pterin oxidation, amplifying local oxidative stress in a ‘feed forward’ process. Within the circulation, increased BH2 is associated with endothelial dysfunction and has been implicated in the pathogenesis of numerous conditions, including pulmonary hypertension [5]. In an IACUC-approved preliminary study of swine that had undergone left upper lobectomy during single lung ventilation 3 days prior to tissue harvest, we measured BH2 and BH4 levels in the non-operated lung and that is maybe different since they actually study the source of the oxidative stress (even from

References


* Corresponding author. Tel.: +1 212 746 2701; fax: +1 212 746 8316. E-mail address: pmheerd@mail.med.cornell.edu
doi:10.1016/j.ejcts.2006.05.022

Reply to the Letter to the Editor
Reply to Heerdt et al.

Panagiotis Misthos*
First Thoracic Surgical Department, ‘SOTIRIA’ General Hospital for Chest Diseases, Athens, Greece

Stylianos Katsaragakis
University of Athens Medical School, First Propaedeutical Surgical Department, Athens, Greece

E-mail address: pmheerd@mail.med.cornell.edu

Received 21 May 2006; accepted 29 May 2006; Available online 20 July 2006

Keywords: Oxidative stress; Lung re-expansion; Postresectional complications

We appreciate the comments of Heerdt et al. [1]. We are delighted that such a prominent group was interested in our study and their preliminary results are qualitatively consistent with ours.

We conducted a prospective analysis in order to investigate the generation of oxygen-free radicals through lipid peroxidation metabolites after one-lung ventilation (OLV) pulmonary resections and to define the contribution of the generated oxygen and nitrogen reactive species on postlobectomy morbidity and mortality [2,3].

The difference concerning the duration of postresectional oxidative stress (12 h vs 72 h) might be explained by the following thoughts: (1) Our results represent the total systematic level of oxidation as it is measured in peripheral blood samples and suggest a common internal antioxidative mechanism of oxygen-free radicals’ clearance and a constant counteraction by the endogenous antioxidant systems. Heerdt et al. reported their results from both the operated and non-operated lung and that is maybe different since they actually study the source of the oxidative stress (even from