Carotid artery stenting in the Zucker rat: a novel, potentially ‘diabetes-specific’ model of in-stent restenosis

AISLING C. MCMAHON, HALA ZREIQAT, HARRY C. LOWE

Dear Sirs,

Both morbidity and mortality from coronary artery disease are higher in patients with diabetes.1 Moreover, percutaneous treatment of coronary artery disease using coronary stents — with either bare metal or the newer drug-eluting stents — is associated with poorer outcomes in patients with diabetes compared to those without, adding to their burden of disease.2 Surprisingly, given these broadly poor outcomes in patients with diabetes, there is a paucity of data using animal models examining the responses to stenting in a diabetic context.3 Such an animal model is proposed below.

Five adult lean Zucker rats underwent stenting of the left common carotid artery. This was performed following an open cutdown under general anaesthesia (using 2% isoflurane) and an arteriotomy. Balloon-mounted human coronary stents (2.0 x 7mm, BiodivYsio, Abbott Vascular, Illinois, US) were placed in the common carotid artery under direct vision (OPMI Pico-microscope, Zeiss, Germany), advanced to a mid-arterial position and deployed at 12 atmospheres. The balloon was then removed, the arteriotomy ligated, and the animals allowed to recover.

There was one peri-operative death, thought to be secondary to anaesthesia. After two weeks, the remaining four animals were sacrificed and the carotids dissected free en bloc. The tissue block was placed in 10% buffered formalin, then plasticised in methylmethacrylate. Sections (100 µm thick) were cut using a band cutting system (Exakt GmbH, Norderstedt, Germany), polished, stained with haematoxylin and eosin and imaged using light microscopy. A representative section is shown (figure 1).

This processing technique leaves individual stent struts in situ. These were observed stretching and compressing, but not lacerating the media, suggesting a mild degree of vessel injury.4 The medial stretch and compression was associated with variable, but concentric, neointima (NI) formation (figure 1). This technique therefore demonstrates the potential to provide a specific model of in-stent restenosis in the setting of diabetes.

Clearly, these are preliminary observations. The degree of NI formation has not yet been quantified in relation to the degree of vessel stretch; the molecular and cellular characterisation of the NI is yet to be elucidated; and the response to drug-eluting stent deployment has not yet been established. However, the technique is straightforward, low cost, readily available and importantly, to our knowledge, the first such description of carotid stenting in the Zucker rat, a readily available animal model of diabetes. In an environment where the clinical need for such models is clear, we trust that these preliminary observations will assist researchers in this important area of investigation.
Acknowledgements
Funding support provided by Diabetes Australia.

Conflicts of interest statement
None declared.

References

ANZAC Research Institute, University of Sydney, and Department of Cardiology, Concord Hospital, Hospital Road, Concord, NSW 2139, Australia.

Aisling C McMahon, Research Scientist
Harry C Lowe, Associate Professor, Cardiology Department

Tissue Engineering and Biomaterials Research Unit, School of Aerospace, Mechanical and Mechatronic Engineering (AMME), University of Sydney, NSW 2006, Australia.

Hala Zreiqat, Research Scientist

Correspondence to: Associate Professor Harry C Lowe
Cardiology Department, Concord Repatriation General Hospital, 3W Multi Building, Hospital Road, Concord, NSW, 2139, Australia.
Tel: + 61 2 9767 3000; Fax: + 61 2 9767 6994
E-mail: h.lowe@unsw.edu.au

Diabetes Vasc Dis Res 2008;5:145–6
doi:10.3132/dvdr.2008.024