Bubbles cause endothelial damage in a positive correlation manner

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Introduction

Decompression sickness (DCS)

- caused by inert gas bubbles formed in tissues and blood vessels due to rapid exposure to reduced ambient pressure [1].

Intravascular bubbles

- a pivotal event in DCS initiating a biochemical cascade including thrombotic events, inflammatory responses and endothelial dysfunction.
- detected by ultrasound in the pulmonary artery have been used as a sign of decompression stress[2].

Endothelial cells

- a multifunctional transducing organ that mediate a plethora of cardiovascular process[3].
- damaged by intravascular bubbles through ischemia/reperfusion, physical contact or by an increase in shear stress[4].
- endothelial damage and dysfunction is considered a useful index of decompression stress.

Purpose of the study

- investigate potential changes in biomarkers of endothelial damage.
- evaluate the relationship between bubble score and the degree of endothelial injury.

Materials and Methods

Animals and groups – Adult male SD rats were assigned to Normal Control group, Standard Decompression group and Rapid Decompression group.

Simulated dive protocol – rats in the standard decompression and rapid decompression group were subjected to 700 kPa air for 90 minutes before decompressing linearly to ambient pressure in 3~5 minutes or in 12 minutes respectively.

Ultrasound detecting and analysis of DCS bubbles– obtained using a Mylab30cv ultrasonic scanner (Esaote, Italy) connected to an ultrahigh frequency (18 MHz) detector. The number of bubbles was scored according to the grading system established by Eftedal OS.

Lung dry/wet weight ratio – fresh specimens were weighted, then were dried in a 60℃ oven for 72 hours, the dry weight was then measured to count the dry-to-wet ratio.

Determination of ET-1, 6-keto-PGF1α, ICAM-1, VCAM-1, MDA and NO – ELISA.

Histology examination – specimens lung in survival rat were soaked in 10% formalin for 48 hours and staining with hematoxylin and eosin.

Statistical analysis of data – Data were analyzed byANOVA with SPSS 17.0. Pearson correlation coefficients were determined to establish the relationship between the changes of these endothelial biomarkers and the score of bubbles presented.

Results

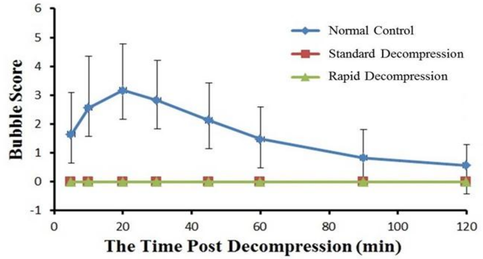

Fig.1 Bubble scores in rat models with different decompression profile: Bubbles were seen solely after rapid decompression,

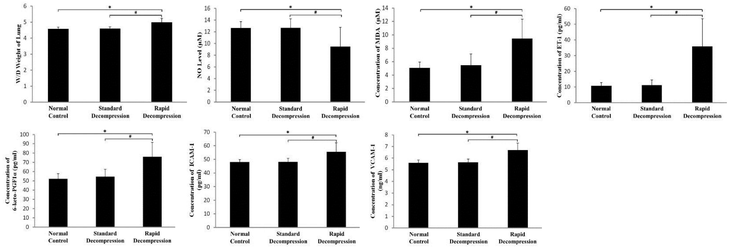

Fig.2 Bubble-induced changes in biomarkers of endothelial damage: Rapid decompression induced a significant increase in lung wet-to-dry weight ratio, ET-1, 6-keto-PGF1α, ICAM-1, VCAM-1 and MDA, while NO showed a significant decrease (* P<0.01 vs Normal Control group, # P<0.01 vs Normal Control group).

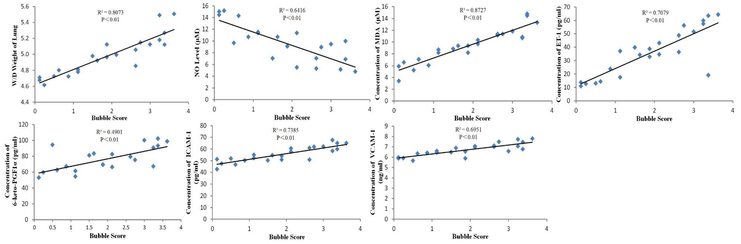

Fig.3 Bubbles cause endothelial damage in a positive correlation manner: In the diving group with rapid decompression, the changes of these endothelial biomarkers correlated positively with the number of bubbles presented (P<0.01).

Results (continued)

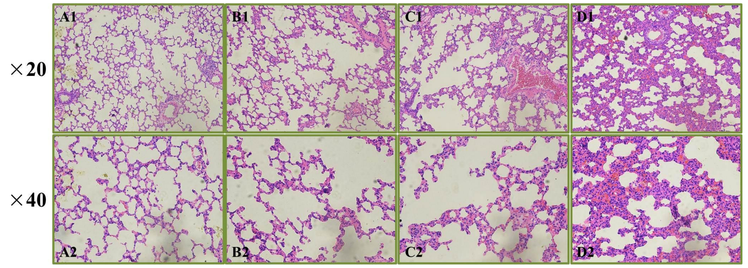

Fig.4 Representative photomicrographs of the lungs in Normal Control (A), Standard Decompression (B), Rapid Decompression with low (C) and high (D) bubble Score: A) Normal histopathology of lung parenchyma; B) Near-normal histopathology of lung parenchyma; C) Histological analysis showed moderate degrees of edema, congestion and leukocyte infiltration; D) Histological analysis showed serious capillary expansion and congestion, as well as more neutrophil infltration into the lung tissue. Lung septum was noticeably thickened.

Conclusion

This study highlights some of the effects of intravascular bubbles on the endothelial cells after rapid decompression. The results suggest that the endothelial damage is mainly caused by bubbles in a positive correlation manner.

Acknowledgement

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References

[1] Evans A et al. *Nature* 222:251-252, 1969.
[2] Levett DZH et al. *Postgrad Med J* 84,*:571-578,* 2008.
[3] Vita JA. *Circulation 127:906-912*, 2011.
[4] Hulst RA et al. *Clin Physiol Funct I* 23:237-246, 2003.