

Aging under pressure:

Exploring interventions to mitigate hypertension risk with a focus on endothelial dysfunction and Reactive Oxygen and Nitrogen Species production

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Abstract: The proportion of adults living with hypertension increases significantly with advancing age. A primary risk factor for the progression of CVD is hypertension, and exploring the factors and processes central to this burden of disease is important for healthy aging. A loss of skeletal muscle quantity and quality occurs with normal aging, resulting in increased peripheral resistance and hypertension. Reactive Oxygen and Nitrogen Species (RONS) are continuously generated in contracting skeletal muscle to allow for essential cellular metabolism, but in excessive amounts can inflict damage to endothelial and skeletal muscle cells. Changes in vascular morphology is an early occurrence in the etiology of CVDs and, while this is a normal characteristic of aging, whether it is a cause or a consequence of aging in hypertension remains unclear. Here we focus on the effects of aging muscle and RONS production, as well as the influence of established and novel interventions to mediate hypertension and CVD risk, and improve health outcomes as we age.

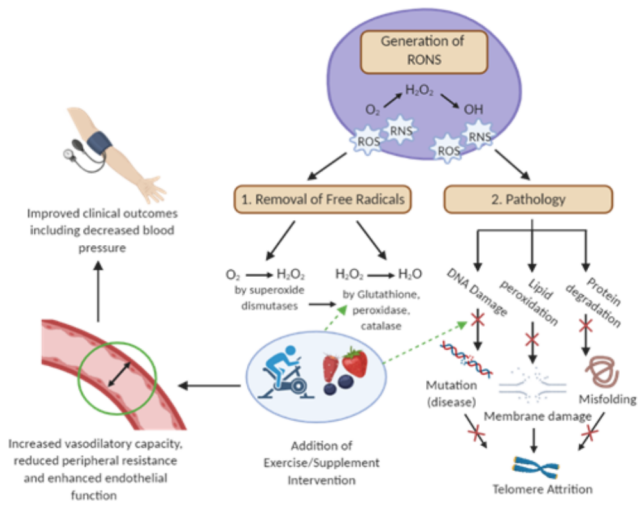


Figure 1. Proposed attenuation of endothelial dysfunction and excessive RONS by the upregulation of antioxidant defenses through the addition of an exercise and/or supplemental dietary intervention. (figure updated from Speer et al. 2020)

Methods: Electronic databases (PubMed, Web of Science and Scopus) were unsystematically searched using the term 'hypertension' in combination with several priori keywords. Findings were discussed in a narrative manner.

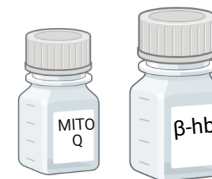
Key Findings:



Aerobic exercise (24-60 mins, 3-5 x per week) enhanced endothelial function and reduced ambulatory BP (-4.9 mmHg SBP and -2.8 mmHg DBP) in medicated hypertensive patients.⁸

The vaso-protective mechanisms of exercise training can play an important role in the modulation of RONS in acute and chronic instances, improving endothelial function and reducing risk for hypertension. While the findings outlined above demonstrate how regular exercise can modulate endothelial function in

hypertensive people, habitual aerobic exercise throughout life could increase vessel health and maintain muscle mass and quality, mediating hypertension risk and associated complications.



Supplementing with compounds that specifically target the mitochondria and induce survival states can decrease oxidative DNA damage⁹ and improve vessel function and arterial stiffness in older people.¹⁰

The consumption of synthesised antioxidant compounds such as MitoQ, or exogenous β -hydroxybutyrate supplemental to the diet, can target excessive mitochondrial RONS and improve blood flow, as well as induce cellular survival mechanisms to lessen the extent of the hallmarks of aging (i.e. telomere attrition and oxidative stress).^{9,10}

We acknowledge that supplements of any kind may not be suitable for all individuals. Further research is needed to establish potential risks associated with, and determine the effectiveness of long-term supplementation of the above compounds at different life stages.

Key points:

- Hypertension remains a prevalent disorder affecting over a third of Australians and incidence increases substantially with age.
- Endothelial dysfunction and excessive RONS production are evident in hypertension and can have ongoing effects if left to escalate.
- Aerobic exercise training can improve NO-induced vasodilatation and decrease BP in hypertensive individuals.
- Supplementation strategies which target the mitochondria or excessive mitochondrial RONS may mitigate age-related vascular dysfunction, reduce BP, and counteract excessive RONS production.
- Additional studies should investigate the quantitative effects of dietary supplementation on RONS production in skeletal muscle, and determine its effectiveness as an acute intervention complementary to exercise at different life stages.

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