Evaluating Empagliflozin in Age Induced Arterial Stiffness

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INTRODUCTION

Arterial stiffness is a hallmark of vascular aging as well as a prognostic marker of future cardiovascular events. Arterial stiffness increases pulse pressure and left ventricular afterload, leading to increased mechanical stress in capillaries potentially leading to damage of highly perfused organs such as the heart and kidneys. Recently, the SGLT2 inhibitor empagliflozin was shown to improve cardiac function in heart failure function, yet its effect on vascular aging is unknown. In the present study, the effect of empagliflozin on arterial stiffness was investigated into further extent.

Figure 1. Representative image of arterial compliance and the dampening capacity of the arterial wall to blood pressure. (Briet et al, 2012)

METHODS

Empagliflozin was administered in vivo to C57Bl6 mice through their drinking water (15mg.kg-1.day-1) for a period of 7 weeks and pulse wave velocity (PWV) was evaluated in vivo. Next, arterial stiffness (Peterson's modulus of elasticity, Ep) was assessed ex vivo in our proprietary oscillating organ bath setup. Additionally regional differences in Ep were assessed in proximal (ascending aorta), central (descending aorta) and a more distal region (infrarenal aorta).

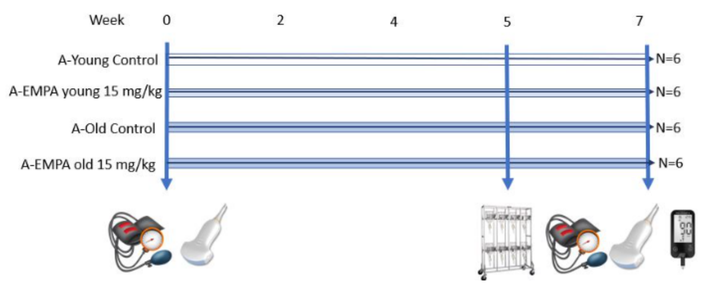

Figure 2. In vivo study design overview. Echocardiography as well as blood pressure was performed at week 0 and week 7 respectively. Metabolic cages were implemented at week 5.

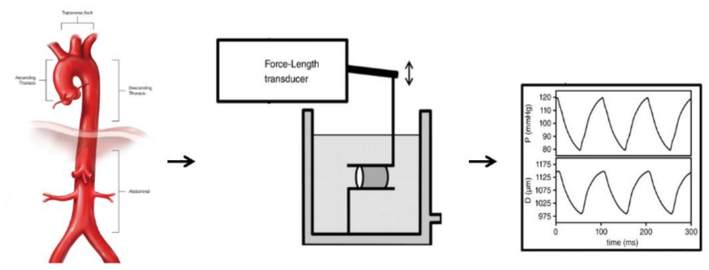

Figure 3. Ex vivo analysis of arterial stiffness. Rodent Oscillatory Tension Set-up for measuring Arterial Compliance (ROTSAC). (Leloup et al, 2016)

CONCLUSION

Our results demonstrate the role empagliflozin plays in attenuating age induced arterial stiffness in the thoracic and infrarenal aorta. Vascular reactivity was also altered under empagliflozin administration young animals.

RESULTS

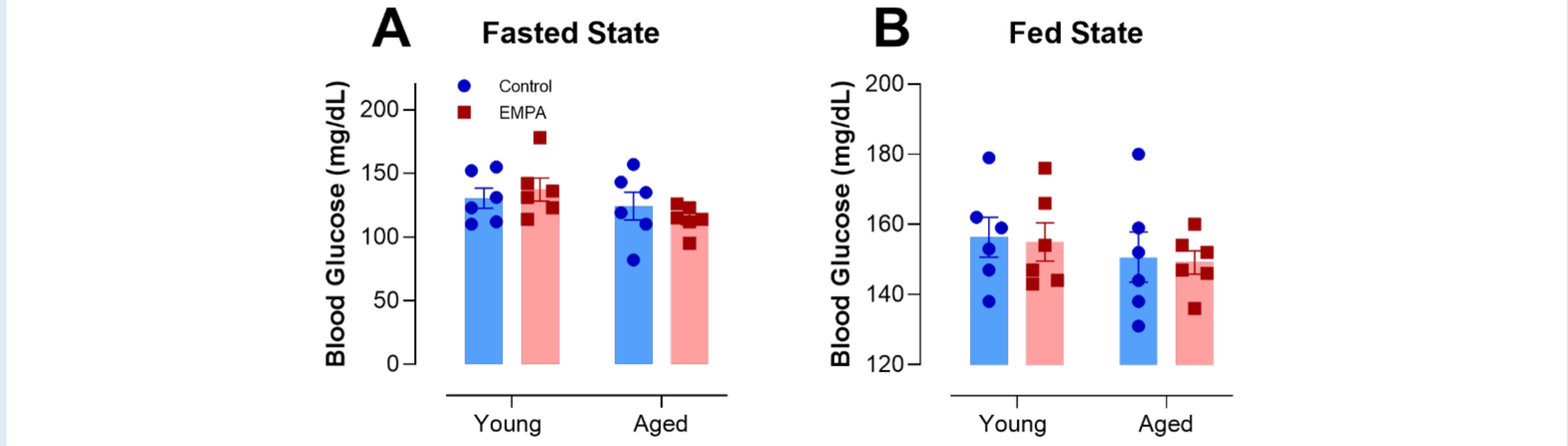

Figure 4. Empagliflozin did not effect blood glucose or PWV values. No differences in blood glucose values were recodered between the young as well as old, control and empagagliflozin treated animals in a fasted state (A) or in a fed state (B). Data is expressed as mean ± SEM, n=6, One-way ANOVA with a Holm-Sidak post hoc test for multiple comparisons. **EMPA** = Empagliflozin, **PWV** = Pulse Wave Velocity.

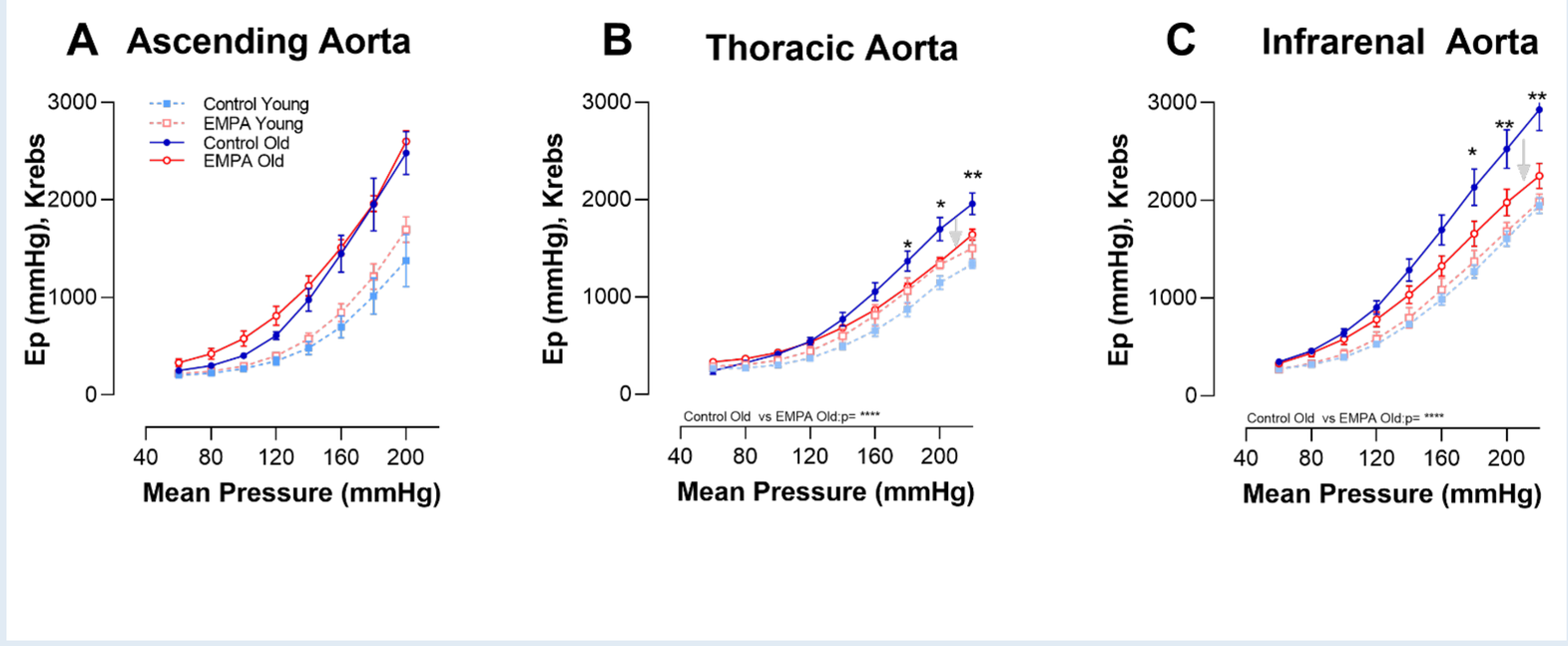

Figure 5. Empagliflozin reduced aged induced arterial stiffness in a region dependent manner *ex vivo*. (A) Non-significant differences were reported in the ascending aorta between control and empagliflozing treated animals. (B) Empagliflozin treated old animals had a significantly (p<.0001) reduced thoracic aorta Ep compared to their age matched controls. (C) Empagliflozin treated old animals had a significantly (p<.0001) reduced infrarenal aorta Ep compared to their age matched controls. Data is expressed as mean ± SEM, n=6, Two-way ANOVA with a Sidak correction test for multiple comparisons. **EMPA** = Empagliflozin, **Ep** = Petersons Modulus.

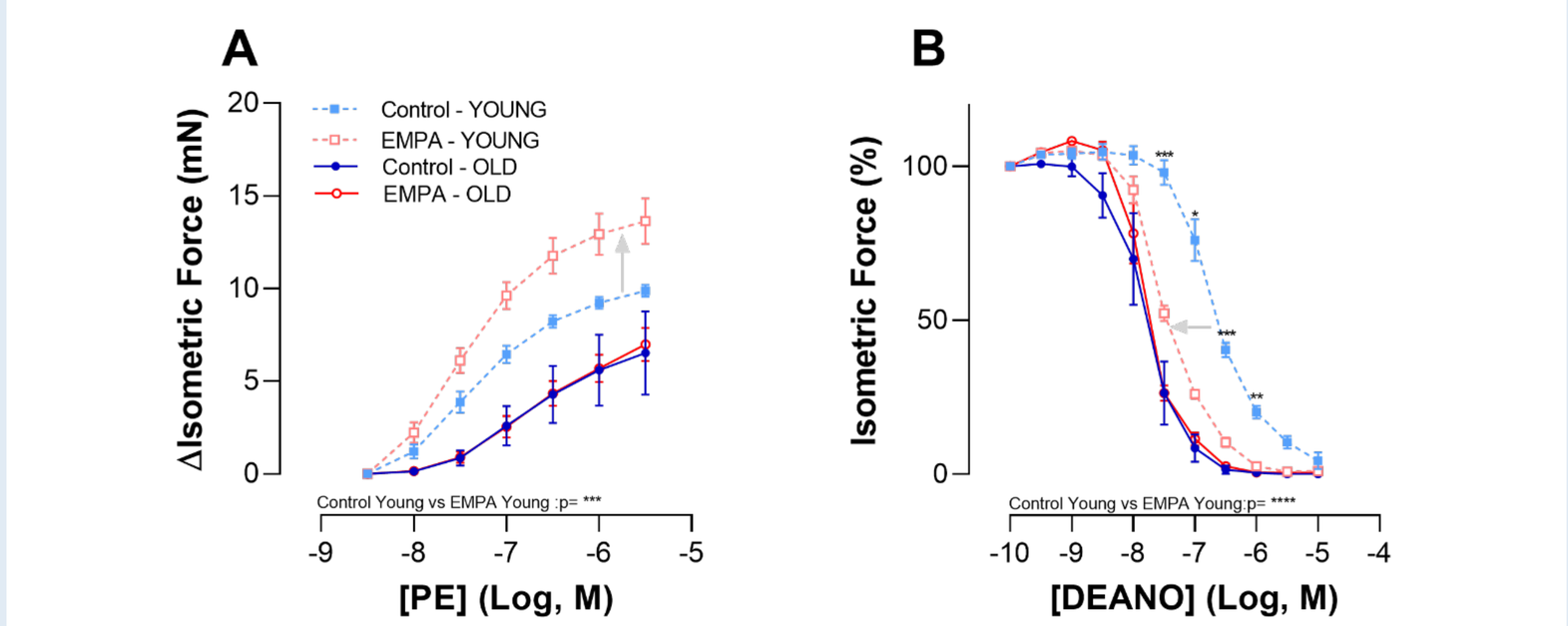

Figure 6. Empagliflozin influenced vascular reactivity comparing young and old treated aortic segments. (A) Empagliflozin treated young animals had a significantly (p<.001) increased isometric force response to phenylephrine compared to their young controls. (B) Empagliflozin treated young animals had a significantly (p<.0001) increased response to the NO donar DEANO compared to their young controls. Data is expressed as mean ± SEM, n=6, Two-way ANOVA with a Sidak correction test for multiple comparisons as well as a One-way ANOVA with a Holm-Sidak post hoc test for multiple comparisons. **EMPA** = Empagliflozin, **MBP** = Mean Blood Pressure, **PE** = Phenylephrine, **DEANO** = Diethylamine Nitric Oxide, **M** = Molar.

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Funded by the EU H2020
Programme MSCA (GA 858070)

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