Influence of Metformin on AAA Derived cells in culture: A Clue to How Metformin slows AAA Growth

Kak Khee Yeung, MD, PhD, FEBVS
Vascular Surgeon & Research Director
Amsterdam University Medical Centers
Amsterdam Cardiovascular Sciences
The Netherlands

Disclosures
Speaker name: Kak Khee Yeung
I have the following potential conflicts of interest to report:
• Dutch Heart Foundation: Dekkerbeurs Senior Clinical Scientist
• W.L. Gore & Associates

Aneurysms and Diabetes
• Epidemiological studies have identified a negative association between AAA and diabetes
• Antidiabetic treatments could also contribute to a protective effect against AAA formation
• Metformin: significant slower AAA growth rate

Metformin
Inflammation
ECM remodeling
Oxidative stress
Reduced AAA development/progression

Studies in patients’ cells are lacking

HOW DOES METFORMIN REDUCE ANEURYSM DEVELOPMENT OR PROGRESSION IN AAA-PATIENTS’ CELLS?

Relationship between metformin and abdominal aortic aneurysm
Juliette Raffort, MD, PhD.1,2,5-Ilaa Massen-Khoudjia, MD. PhD.1,2,5-Elaine Jeun-Bacceci, MD. PhD.1,2,5 and Hubert Latrille, MD, PhD.2,3,5—Nantes, France

ABSTRACT
Abdominal aortic aneurysm (AAA) is a life-threating disease and pharmacologic agents to treat the disease remain lacking for clinical practice. Epidemiologic studies have identified a negative association between the use of antidiabetic drugs, including metformin, and AAA. Metformin is well known for its blood glucose-lowering effect, but its action on both mesentery and inflammatory response has led to propose it as a potential therapeutic target in several cardiovascular diseases. In this review, we summarize the current knowledge on the link between metformin and AAA.

Based on the known effects of the drug on the aortic wall, translational applications and clinical trials investigating the effects of metformin in the management of patients with AAA are discussed. (J Vasc Surg 2019;70:777) Key words: Abdominal aortic aneurysm; Metformin; Biguanides; Antidiabetic drug; Clinical trial

• 6 patient cohort studies → effect of metformin on AAA development
• Experimental models → effect on expression of ECM proteins

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Mechanisms of anti-AAA actions

- Metformin
- Fibrinogen
- F-actin
- AIM2
- Ficylin-1

mRNA: Metformin has an anti-inflammatory function in SMC

mRNA: Less suppression of cell proliferation by TP53 in SMC after treatment with metformin

AIM2 is upregulated in cells treated with metformin, + SMC proliferation

Even more SMC proliferation activated by Metformin in AAA-patient SMC
Conclusion

- Metformin reduces the inflammation, activates the inflammasome and stimulates SMC proliferation in AAA-patients

- 3D and 4D bio-engineered vessels with patient-specific cells

- Clinical Trials