

Pathophysiologie der Aortenstenose

Federico Moccoetti
OA mbF Kardiologie
Luzerner Kantonsspital

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Kompetenz, die licheit.

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Statine

- SALTIRE (n=77) randomisiert Atorvastatin 80mg vs Placebo. Outcome: Progression (TTE)
- SEAS (n= 1873) randomisiert Simvastatin+Ezetimib vs. Placebo. Outcome: Kardiovaskuläre Events inkl. Aortenklappenersatz
- ASTRONOMER (n=269) Rosuvastatin 40mg vs. Placebo. Outcome: Progression (Gradient)
- Metaanalyse aus TNT, IDEAL SPARCL (Atorva 80mg vs 10mg): keine Unterschiede in Inzidenz

Cohen S.J. et al., A Randomized Trial of Intensive Lipid-Lowering Therapy in Patients With Aortic Stenosis, NEJM 2010
Rosenthal AB et al., Intensive Lipid Lowering with Simvastatin and Ezetimibe in Aortic Stenosis, NEJM 2008
Chen H. et al., Effect of Lipid Lowering With Rosuvastatin on Progression of Aortic Stenosis, Circulation 2010
Anavekar N.J. et al., Impact of High-Dose Atorvastatin Therapy and Clinical Risk Factors on Incident Aortic Valve Stenosis in Patients With Cardiovascular Disease from TNT, IDEAL, and SPARCL, Am J Cardiol 2014

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Risikofaktoren

- Hypertonie, Diabetes, Dyslipidämie
- Adipositas
BMI >30Kg/m2 erhöht das Risiko 2x
- Niereninsuffizienz
eGFR<30ml/min erhöht das Risiko 2x

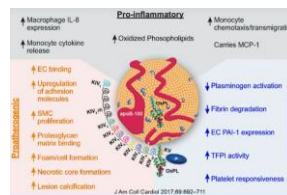


Yan et al., Association Between Cardiovascular Risk Factors and Aortic Stenosis, JACC 2017
Larsson SC, et al. Body mass index in relation to cardiovascular conditions, in the UK Biobank, Eur Heart J 2019
Vavala C et al., Kidney Dysfunction and the Risk of Developing Aortic Stenosis, JACC 2018

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Lipoprotein "klein a" – Lp(a)

- ApoB 100 (wie LDL)
- Oxydierte Phospholipide (wie LDL)
- Zusätzlich Apo(a)
 - Ähnlich zu Plasminogen (inhibiert Plasmin)
- Genetisch bestimmt
- Assoziiert mit Aortenstenose



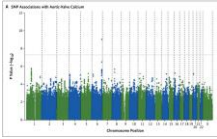
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Lp(a) Genomwide Association Studie (GWAS)



Table 1. Genomwide Significant Associations of Single Nucleotide Polymorphisms (SNPs) with Aortic Valve and Mitral Annulus Calcification*

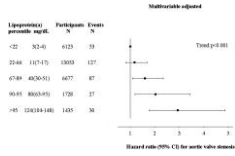
SNP	Phenotype	Chromosome	Minor Allele	Major Allele	OR (95% CI)	P Value	No. of Studies	Report Gene
r1045357	Aortic valve calcification	5	G	C	2.05 (1.43-3.13)	8.5e-07**	3	LPA



Thanassoulis G et al., Genetic Associations with Valvular Calcification and Aortic Stenosis. NEJM 2013

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Stark erhöhtes Lp(a) mit 3x höheres Risiko für Aortenstenose assoziiert



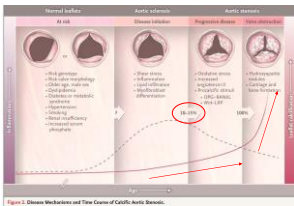
Kamstrup PR et al., Elevated Lipoprotein(a) and Risk of Aortic Valve Stenosis in the General Population. JACC 2014

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Progression

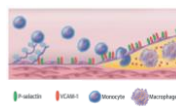


Choi KM et al., Aortic Valve Stenosis — From Patients at Risk to Severe Valve Obstruction. NEJM 2014

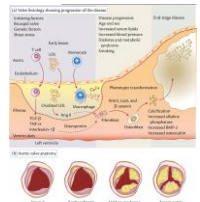
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Atherosklerose



Aortenstenose

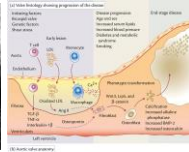
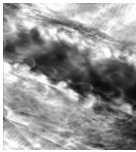
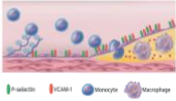


Mocavi F et al., Myocardial Infarction Promotes Sustained Proinflammatory Endothelial Activation in Remote Arteries. JACC 2018

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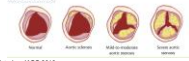
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Atherosklerose



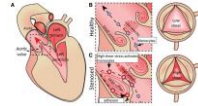
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Aortenstenose



Mocetti F et al., Myocardial Infarction Produces Sustained Proinflammatory Endothelial Activation in Remote Arteries. JACC 2018

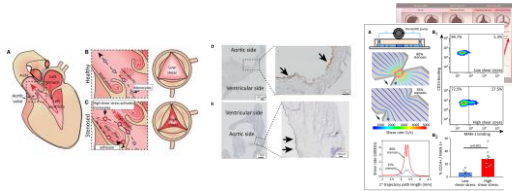
Beschleunigte Progression – neue Erkenntnisse



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Baratchi S et al., TAVI Represents an Anti-Inflammatory Therapy Via Reduction of Shear Stress-Induced, Piezo-1-Mediated Monocyte Activation. Circulation 2020

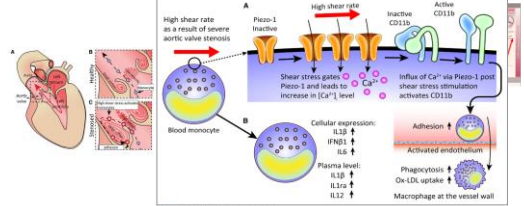
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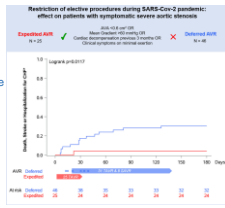
Baratchi S et al., TAVI Represents an Anti-Inflammatory Therapy Via Reduction of Shear Stress-Induced, Piezo-1-Mediated Monocyte Activation. Circulation 2020

Eine "unethische" Studie

- Outcome:
- HR 0.12 (0.01-0.60)

Events Dekompensation-driven in der Deferred-Gruppe

- Dekompensation 22%
- Tod 4%
- Stroke 6%



Lanz J et al., Deferred versus Expected Aortic Valve Replacement in Patients with Symptomatic Severe Aortic Stenosis During the SARS-CoV-2 Pandemic, Global Heart 2020

Take Home Messages

- Kein degenerativer "wear and tear" sondern aktiver Prozess (Risikofaktoren, Inflammation, Verkalkung), ähnlich zur Atherosklerose
- Im Verlauf der Erkrankung übernimmt Shear Stress die Führung
- Keine "medical therapy" in Sicht (mindestens kurz-mittelfristig)
- Nach Symptombeginn zeitnah Klappenersatz (AKE oder TAVI) sinnvoll
- Aortenklappenersatz verhindert kardiovaskuläre Ereignisse (insbesondere Herzinsuffizienz)

Vielen Dank für die Aufmerksamkeit!



Dr. med. Federico Moccetti
OA mbF Kardiologie
Herzszentrum Luzerner Kantonsspital
Spitalstrasse
6000 Luzern 10
E-Mail: federico.moccetti@luks.ch
Tel.: 041 205 14 79