

Understanding and Managing Obesity-Related HFpEF

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Obesity Is the Very Heavy Elephant in the Middle of the Room

- Obesity is a major determinant or exacerbating factor in heart failure.
 - 40-45% of HF_rEF
 - 75-85% of HF_pEF
- Interventions that cause weight loss reduce the risk of heart failure; those that cause weight gain increase the risk of heart failure.

Not All Obesity Is Alike: We Care About Biologically Active Fat



Visceral adiposity (especially epicardial fat)

Abdominal obesity (based on waist circumference):
> 102 cm in men and > 88 cm in women

Increased body mass index

Why Does Obesity Play Such an Important Role in Heart Failure?

- Exaggerated demand on heart to move increased mass through space
- Adipose tissue — especially visceral fat — is biologically active, both as a source of hormones (adipokines) and a source of systemic inflammation

There Are Two Phenotypes of Heart Failure With a Preserved Ejection Fraction in Obese People

	Normal or high-output heart failure in obese people	Obesity-related heart failure with a preserved ejection fraction
Age	Typically middle-aged	Typical more elderly
Gender	Men = women	Women >> men
Body mass index	Markedly increased ($\approx 35\text{-}45 \text{ kg/m}^2$)	Markedly increased ($\approx 35\text{-}45 \text{ kg/m}^2$)
Atrial fibrillation	< 5%	60-70%
LV end-diastolic dimension	Meaningfully increased	Modestly increased
Echo E/e'	Abnormally increased	Abnormally increased
Natriuretic peptides	Markedly increased (NTproBNP $\approx 1000 \text{ pg/ml}$)	Modestly increased (NTproBNP $\approx 200 \text{ pg/ml}$)
Proinflammatory biomarkers and comorbidities	Not increased	Increased
eGFR	Normal or somewhat increased for age	Moderately to severely decreased

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Obesity with systemic inflammation



Adipose tissue expansion and secretion of proinflammatory adipocytokines



End-organ inflammation, fibrosis and microvascular dysfunction

Epicardium



Epicardial fat

Ventricular myopathy



Decreased LV distensibility



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Obesity with systemic inflammation

Epicardial adipose tissue expansion and secretion of proinflammatory adipocytokines

End-organ inflammation, fibrosis and microvascular dysfunction

Atrial myopathy

Ventricular myopathy

Atrial fibrillation

Impaired eGFR

Decreased LV distensibility

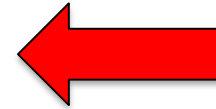
Heart failure with preserved ejection fraction

Perirenal fat

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Heart failure with preserved ejection fraction

What Proinflammatory Mediators Are Secreted by Dysfunctional Epicardial Fat?

Proinflammatory cytokines

- Tumor necrosis factor- α
- Interleukin 1- β
- Interleukin 6

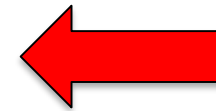
Adipogenic hormones

- Leptin
- Neprilysin
- Aldosterone

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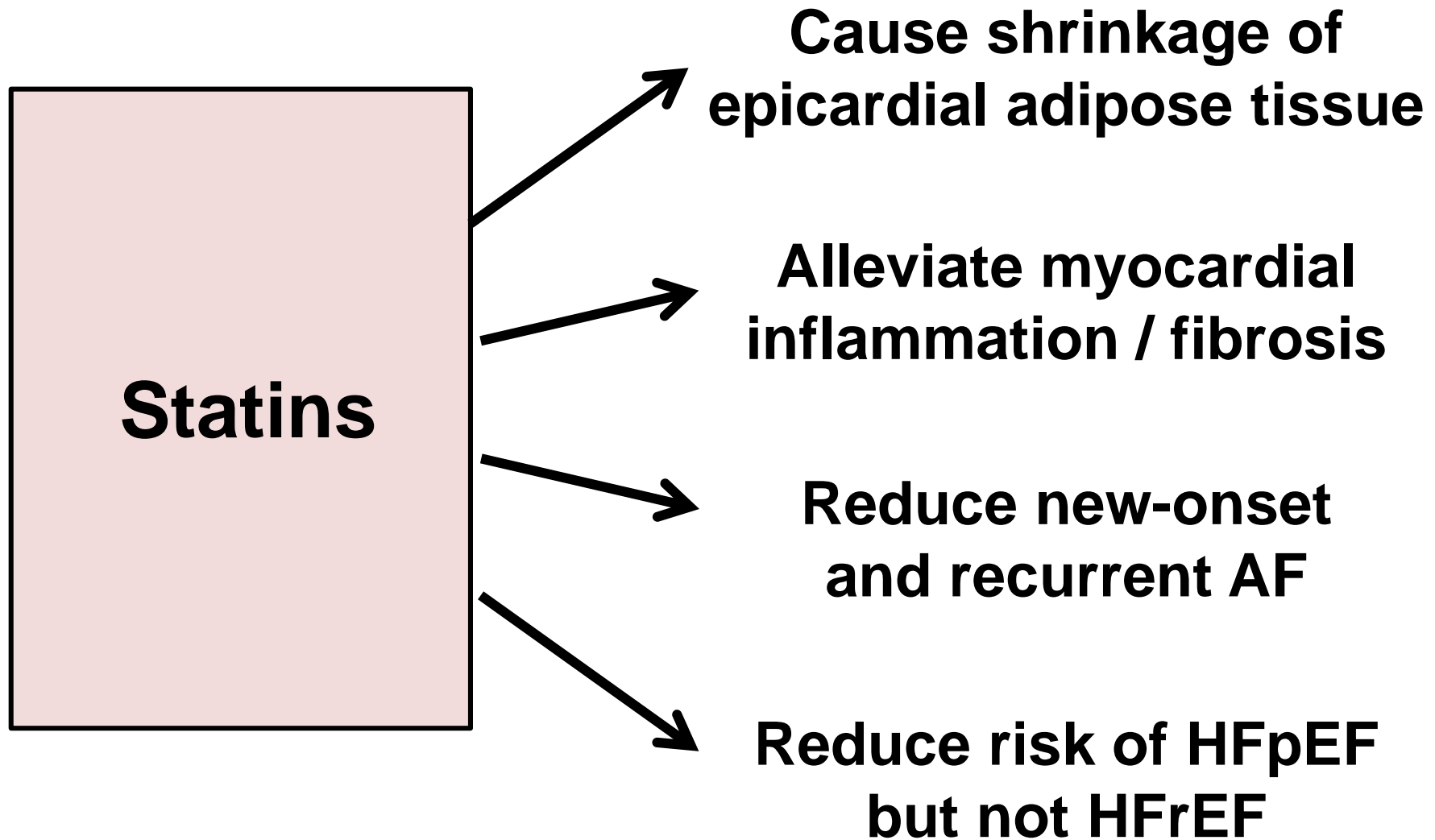
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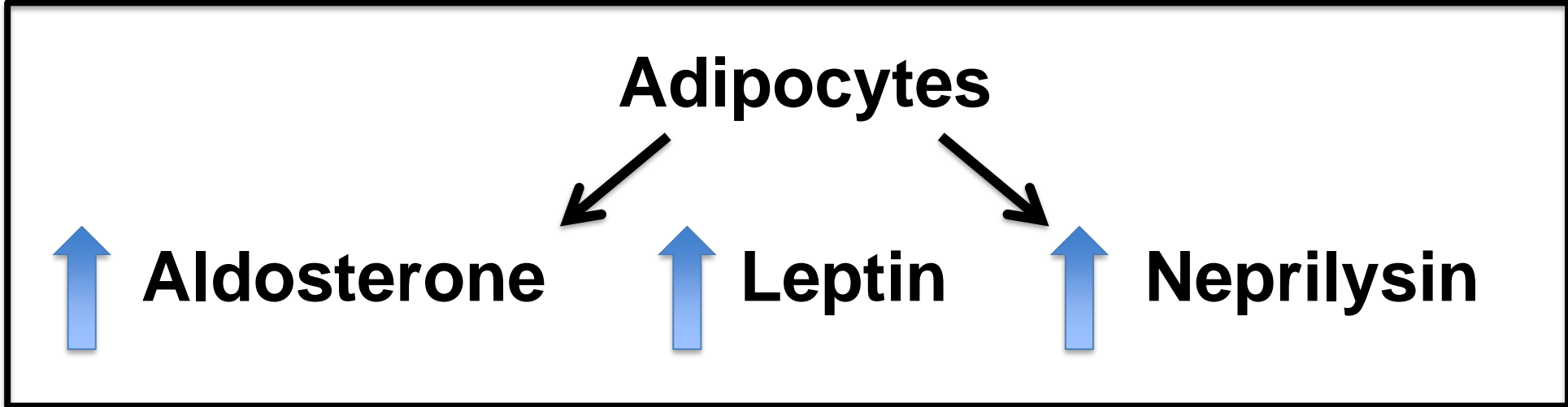
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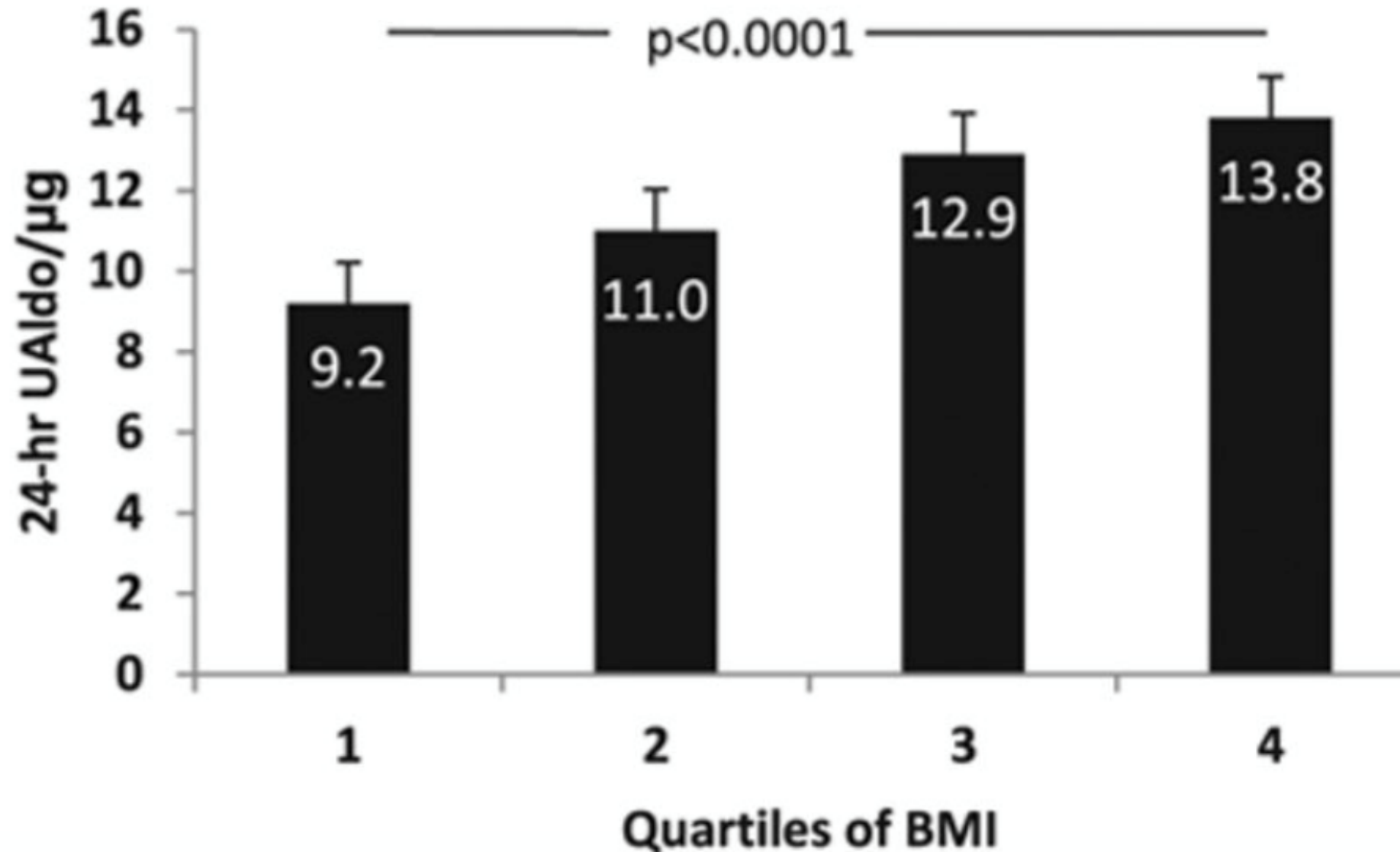
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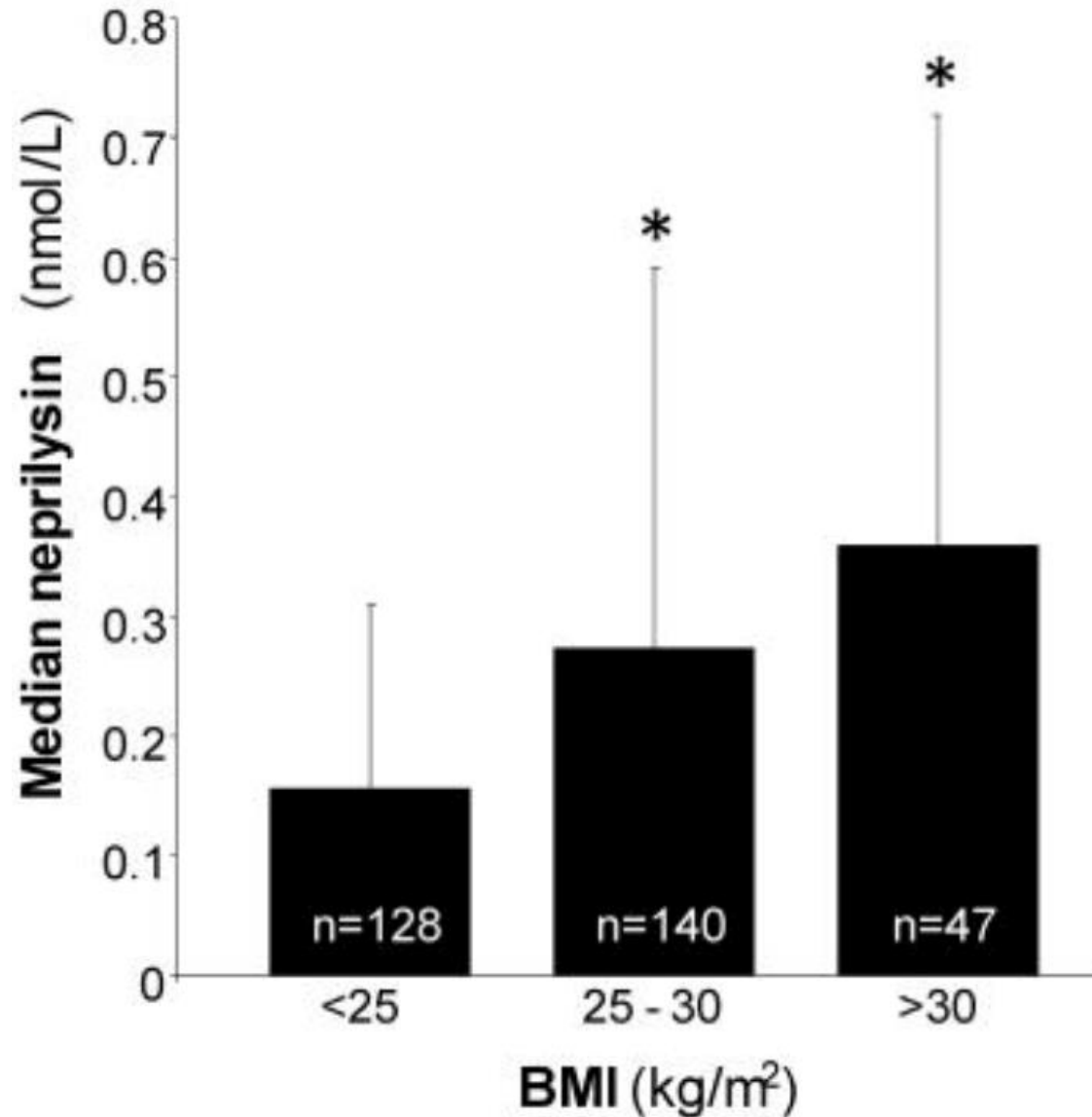
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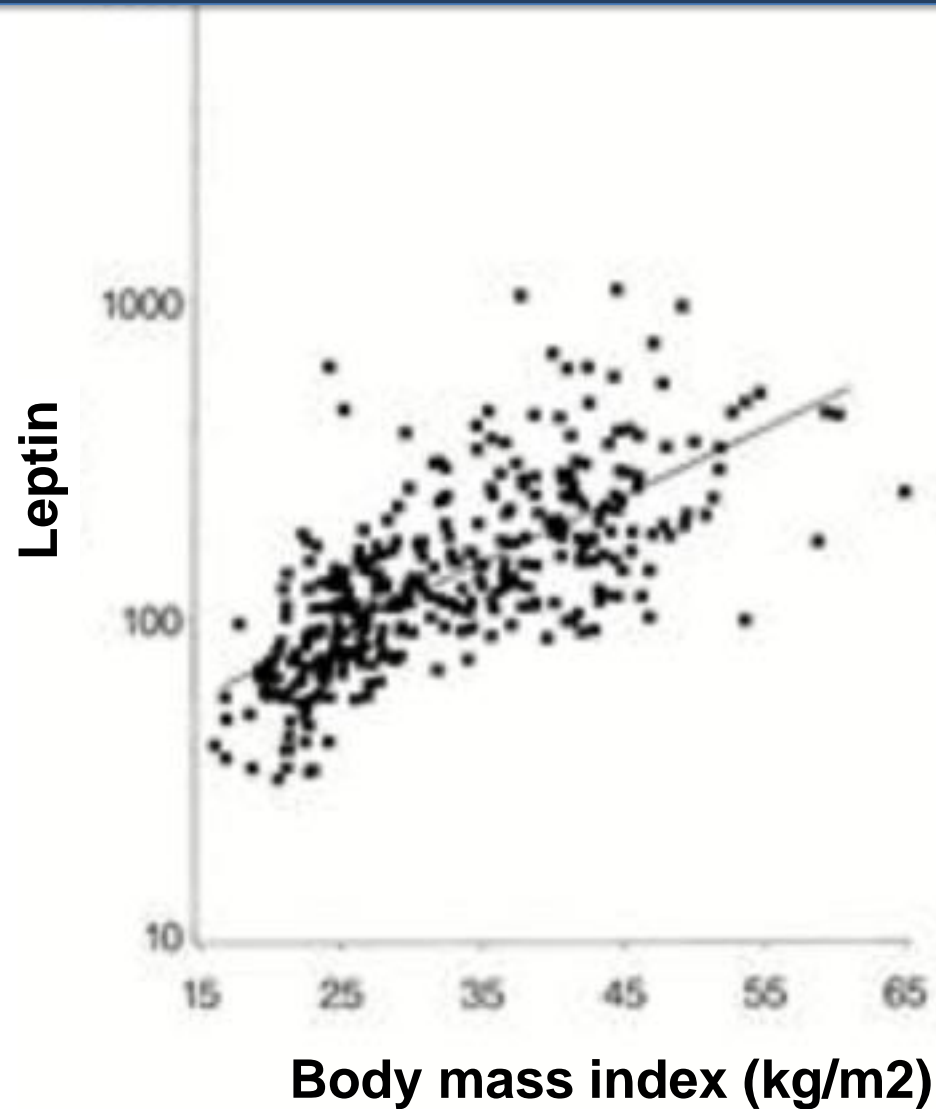
Direct Relationship Between Body Mass Index and Aldosterone

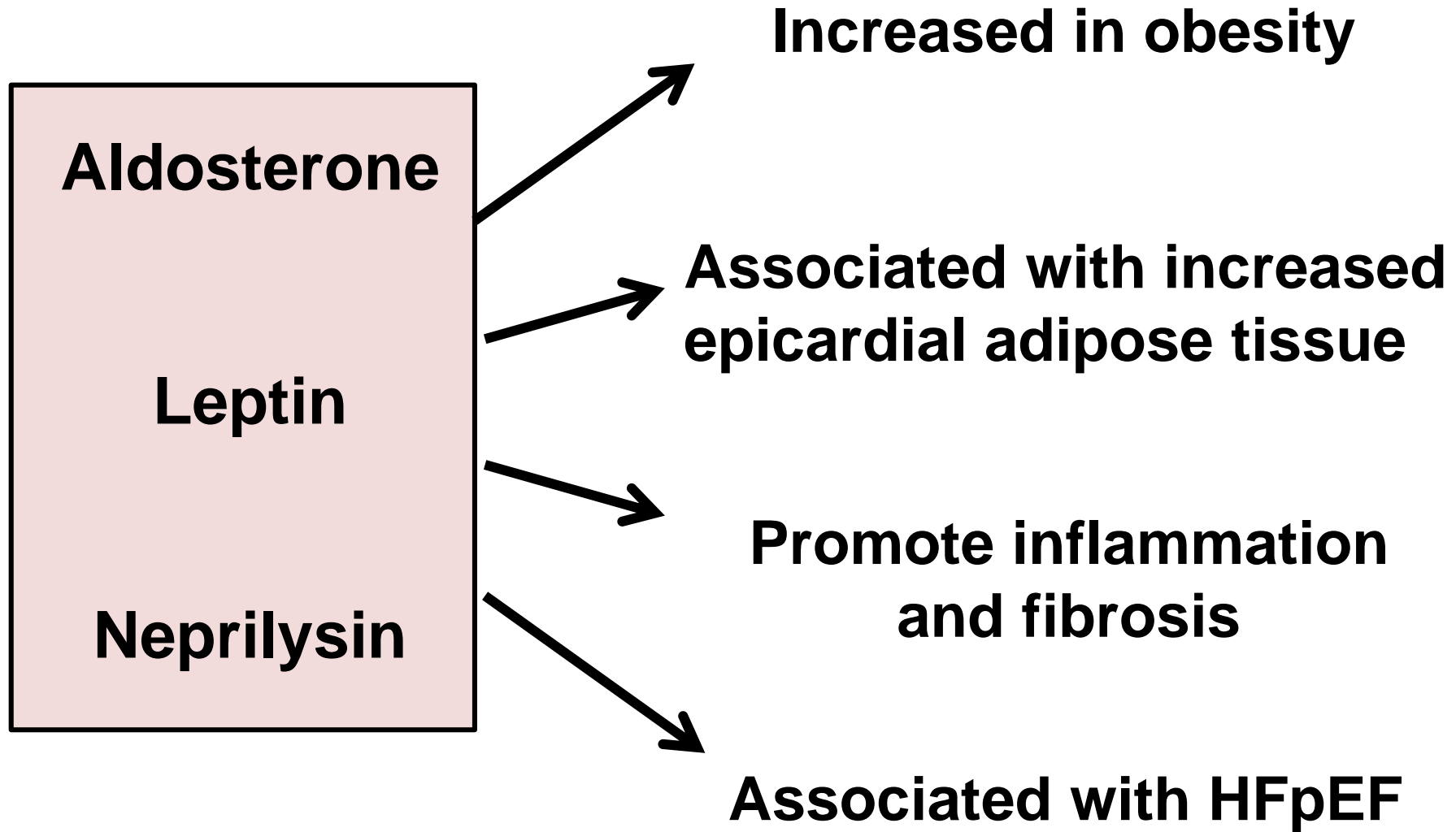


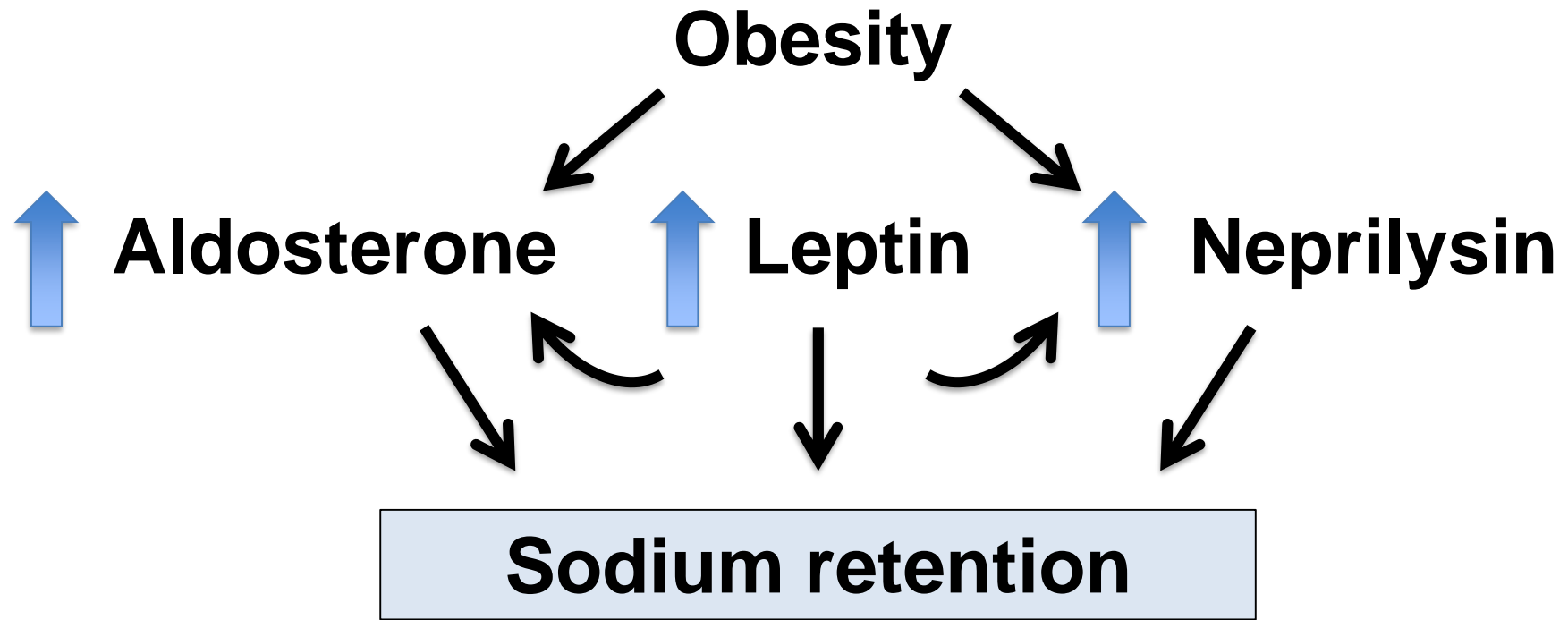
Direct Relationship Between Body Mass Index and Neprilysin



Direct Relationship Between Body Mass Index and Leptin







Obesity-Related HFpEF Differs From Other HFpEF Because Body Mass Drives Sodium Retention

