Insulin resistance and atrial fibrillation

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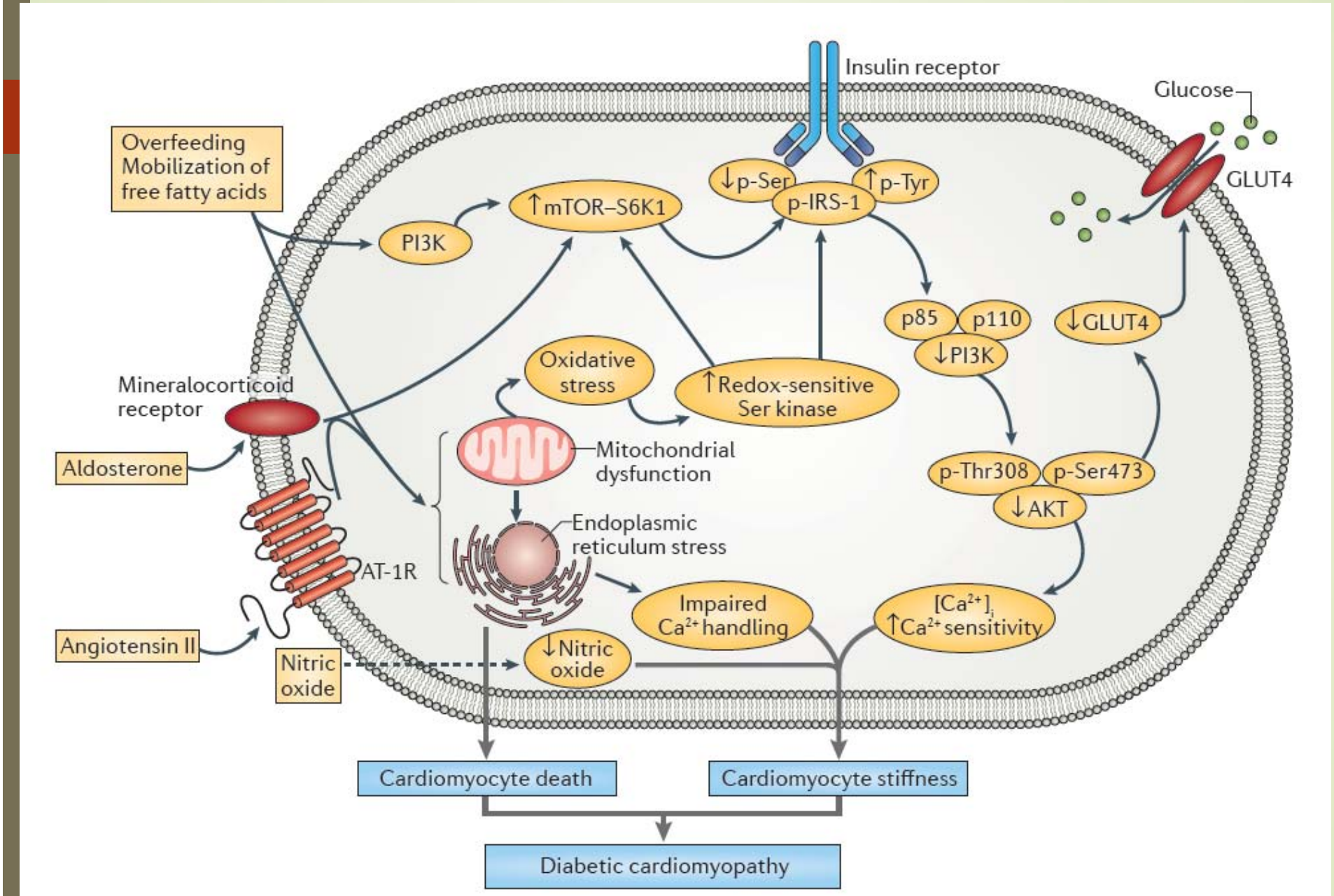
- Insulin resistance (IR) is characterized by reduced insulin signaling and reduction in glucose transport of cells, associated with a compensatory increase in pancreatic production of insulin that results in hyperinsulinemia
- IR is often associated with the cardiorenal metabolic syndrome, a series of interacting conditions including diabetes, hypertension, hyperlipidemia, chronic kidney disease and heart failure.



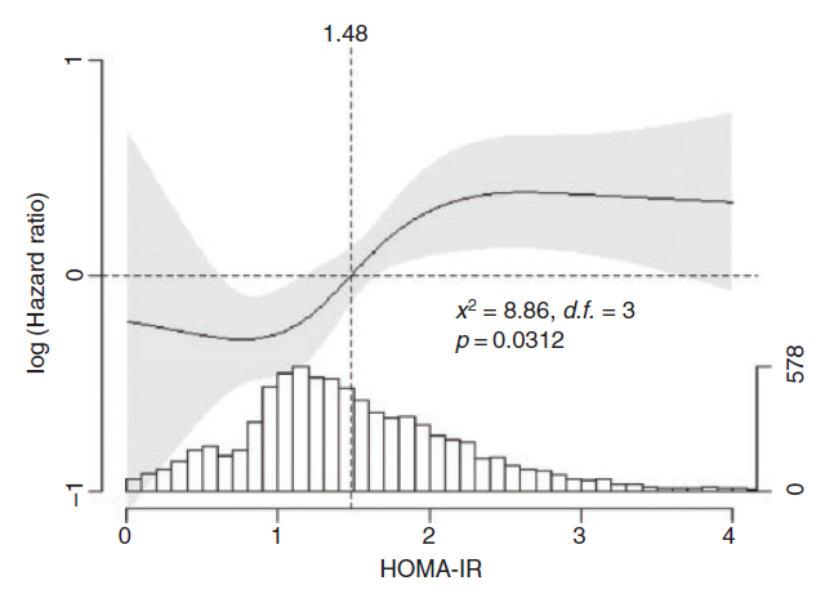
Nat Rev Endocrinol . 2016;12(3):144

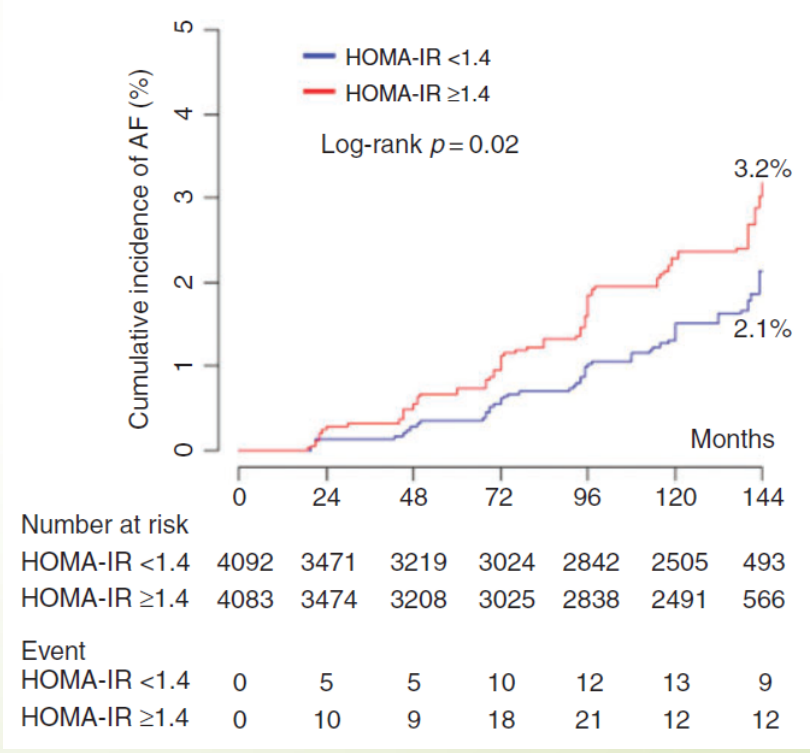
Insulin resistance and AF

- Several studies have reported the association of AF with metabolic syndrome, which is characterized by high IR.
- Cardiovasc Diabetol 2021;20(1):20
- Previous studies from Western countries have failed to demonstrate an independent association between IR and AF.
- Am J Cardiol 2012; 109: 87–90
- Nutr Metab Cardiovasc Dis 2018; 28: 716–721.
- Recently it was reported from Korea there is an independent association between IR and AF in a nondiabetic Korean longitudinal cohort.
- European Journal of Preventive Cardiology 2020;27(18):1934–41

Association between insulin resistance and risk of atrial fibrillation in non-diabetics

Yonggu Lee[1,*], Sung Joo Cha[2,*], Jung-Hwan Park[3,*], Jeong-Hun Shin[1], Young-Hyo Lim[2], Hwan-Cheol Park[1], Jinho Shin[2], Chun Ki Kim[4] and Jin-Kyu Park[2]

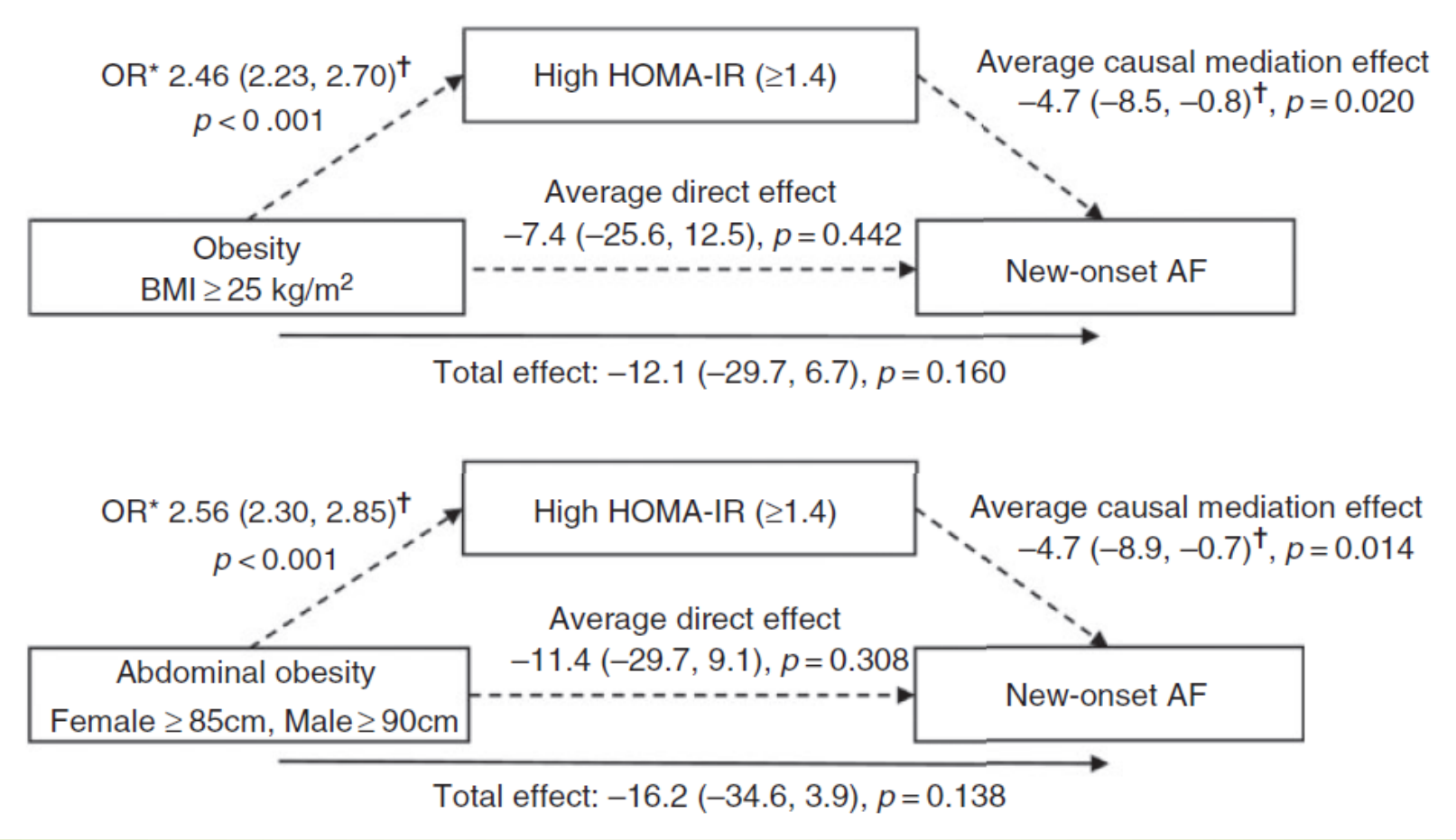




Number at risk							
HOMA-IR <1.4	4092	3471	3219	3024	2842	2505	493
HOMA-IR ≥1.4	4083	3474	3208	3025	2838	2491	566
Event							
HOMA-IR <1.4	0	5	5	10	12	13	9
HOMA-IR ≥1.4	0	10	9	18	21	12	12

European Journal of Preventive Cardiology 2020;27(18):1934

High HOMA-IR levels significantly mediated the impact of obesity on AF development, whereas obesity itself did not directly, or increase the risk of AF.



European Journal of Preventive Cardiology 2020;27(18):1934

ORIGINAL INVESTIGATION Open Access

Atrial fibrillation and its arrhythmogenesis associated with insulin resistance

Yi-Hsin Chan[1,2,3], Gwo-Jyh Chang[5], Ying-Ju Lai[7], Wei-Jan Chen[1,2], Shang-Hung Chang[1,2,4], Li-Man Hung[6], Chi-Tai Kuo[1,2*†] and Yung-Hsin Yeh[1,2*†]

- Insulin resistance (IR) is considered as a risk factor for atrial fibrillation (AF) even before diabetes develops.
- The pathophysiology and underlying mechanism are largely unclear.
- We investigated the corresponding mechanism in IR rat model
- AF was evaluated and induced by burst atrial pacing. Isolated atrial myocytes were used for whole-cell patch clamp and calcium assessment. Ex vivo whole heart was used for optical mapping.

overweight | non-overweight

	Control (n = 30)	HFa (n = 30)	HFr (n = 30)
0-week body weight (g)	305 ± 13.4	297 ± 8.2	293 ± 9.5
12-week body weight (g)	547 ± 55.8	678 ± 49.4*	555 ± 50.2
HW/BW (mg/g)	2.8 ± 0.5	2.4 ± 0.2*	2.8 ± 0.5
HR (bpm)	355 ± 10.2	380 ± 9.5	378 ± 8.5
MAP (mmHg)	77 ± 14.2	98 ± 9.9*	101 ± 14.3*
Blood glucose (mg/dL)	164 ± 19.9	196 ± 46.8*	214 ± 46.4*
Insulin (μg/L)	1.8 ± 0.9	4.6 ± 1.5*	4.3 ± 2.3*
Triglyceride (mg/dL)	59 ± 17.7	117 ± 38.8 *	118 ± 37.7*
Cholesterol (mg/dL)	75 ± 12.9	96 ± 9.5*	119 ± 25*
HDL (mg/dL)	27.5 ± 4.3	24.7 ± 3.8	32.8 ± 7.1*
HOMA-IR	24.3 ± 10.5	41.9 ± 12.1*	36 ± 12.5*

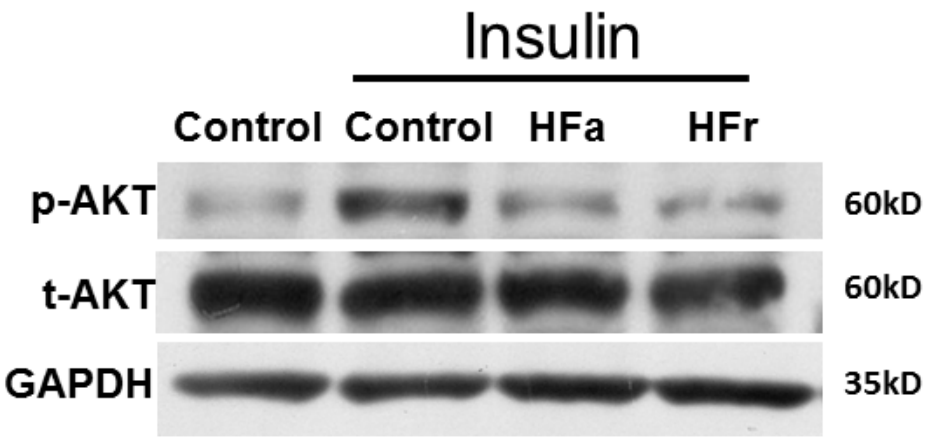
HW heart weight, *BW* body weight, *MAP* mean arterial pressure, *HDL* high-density lipoprotein

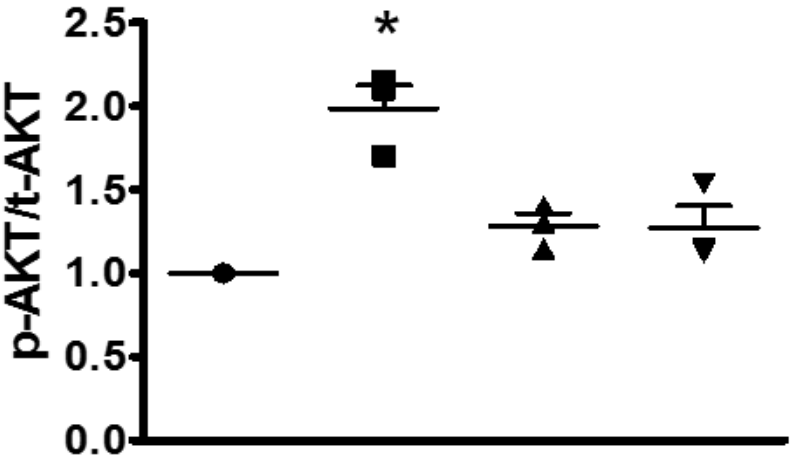
HOMA-IR = glucose (mg/dL) × insulin (mIU/L)/405

- Two rat insulin resistance model: (1) overweight rat by high fat diet (2) non-overweight rat by high fructose diet

Cardiovasc Diabetol 2019;18:125

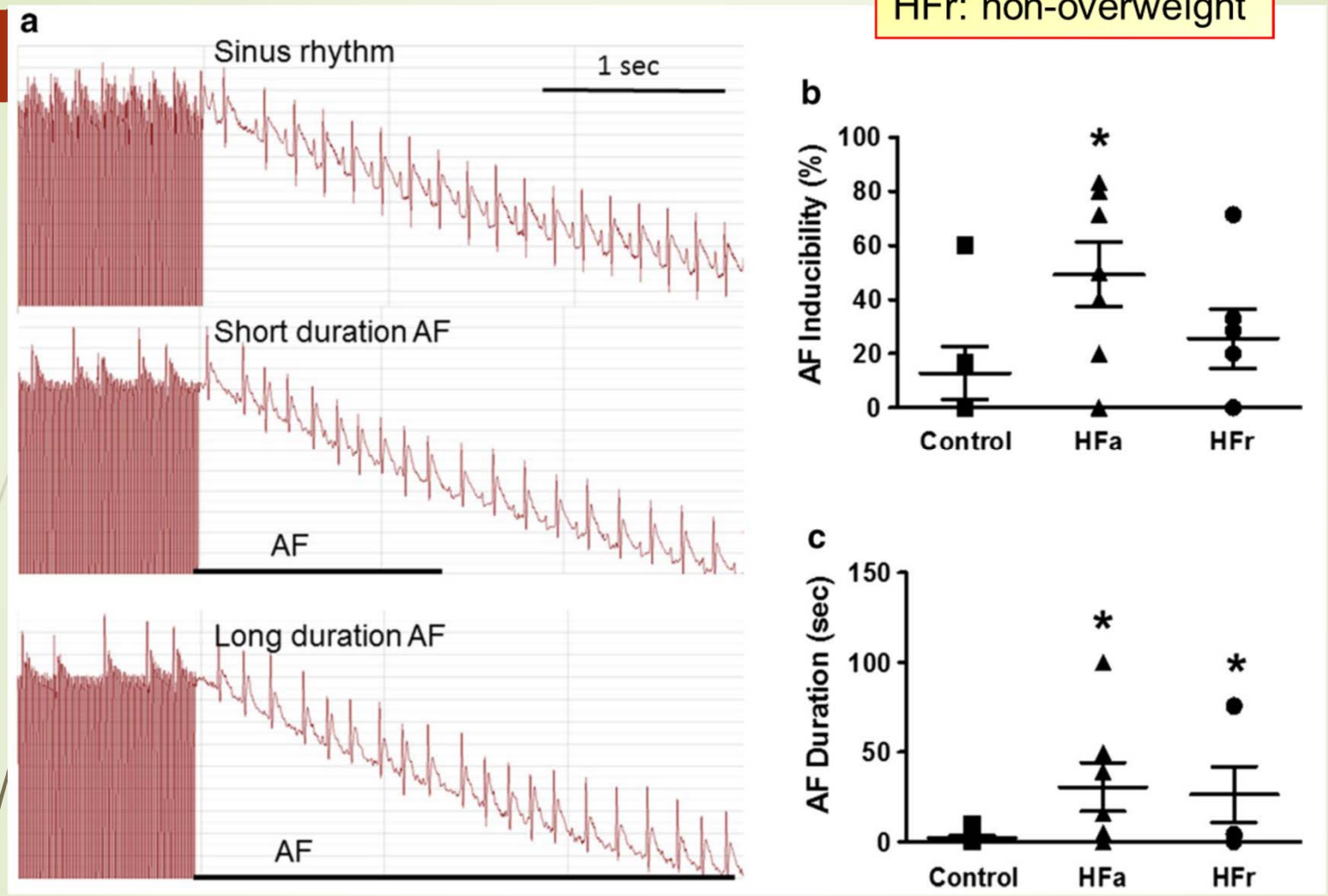
overweight | non-overweight





Cardiovasc Diabetol 2019;18:125

HFa: overweight
HFr: non-overweight



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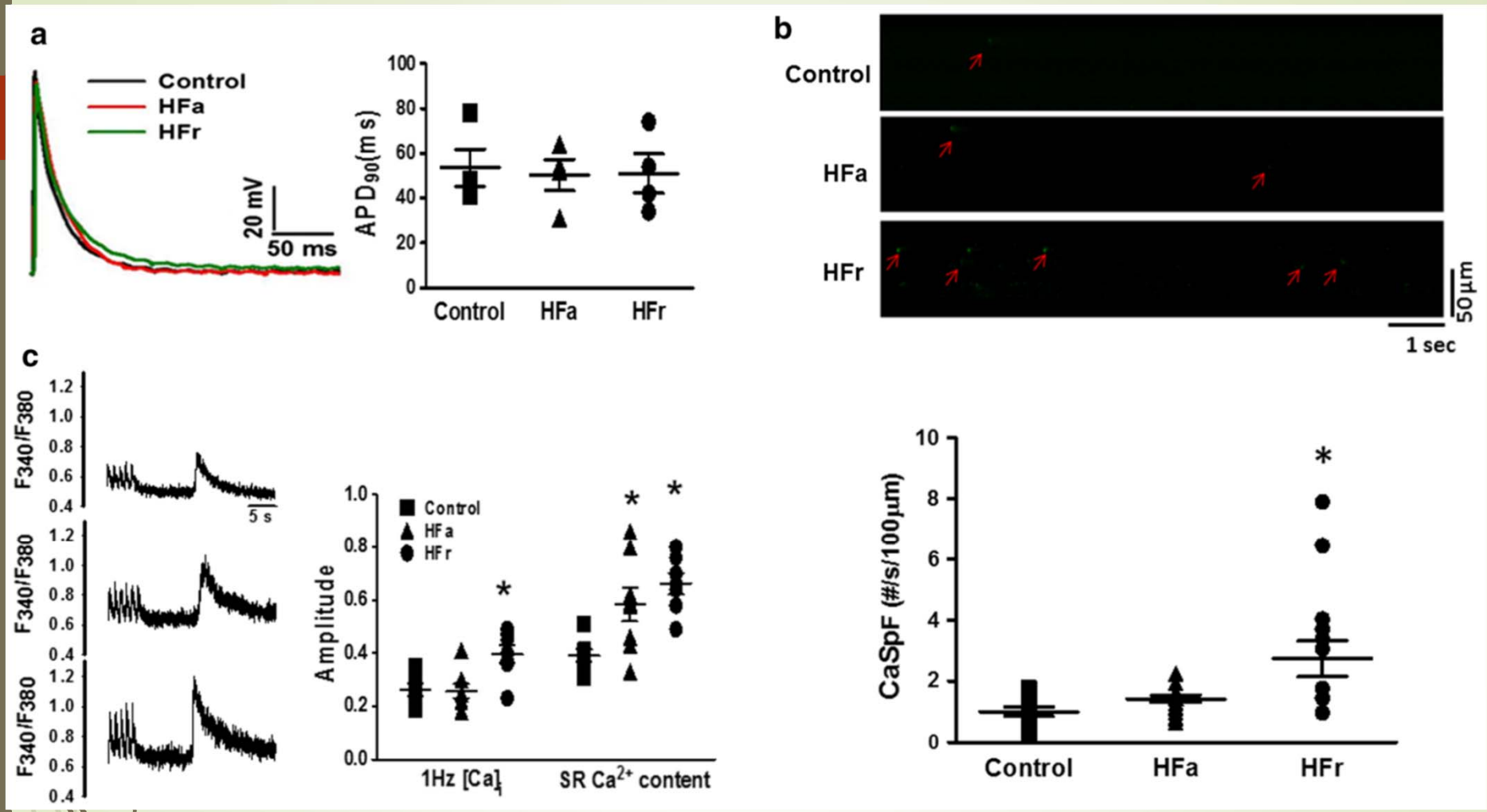

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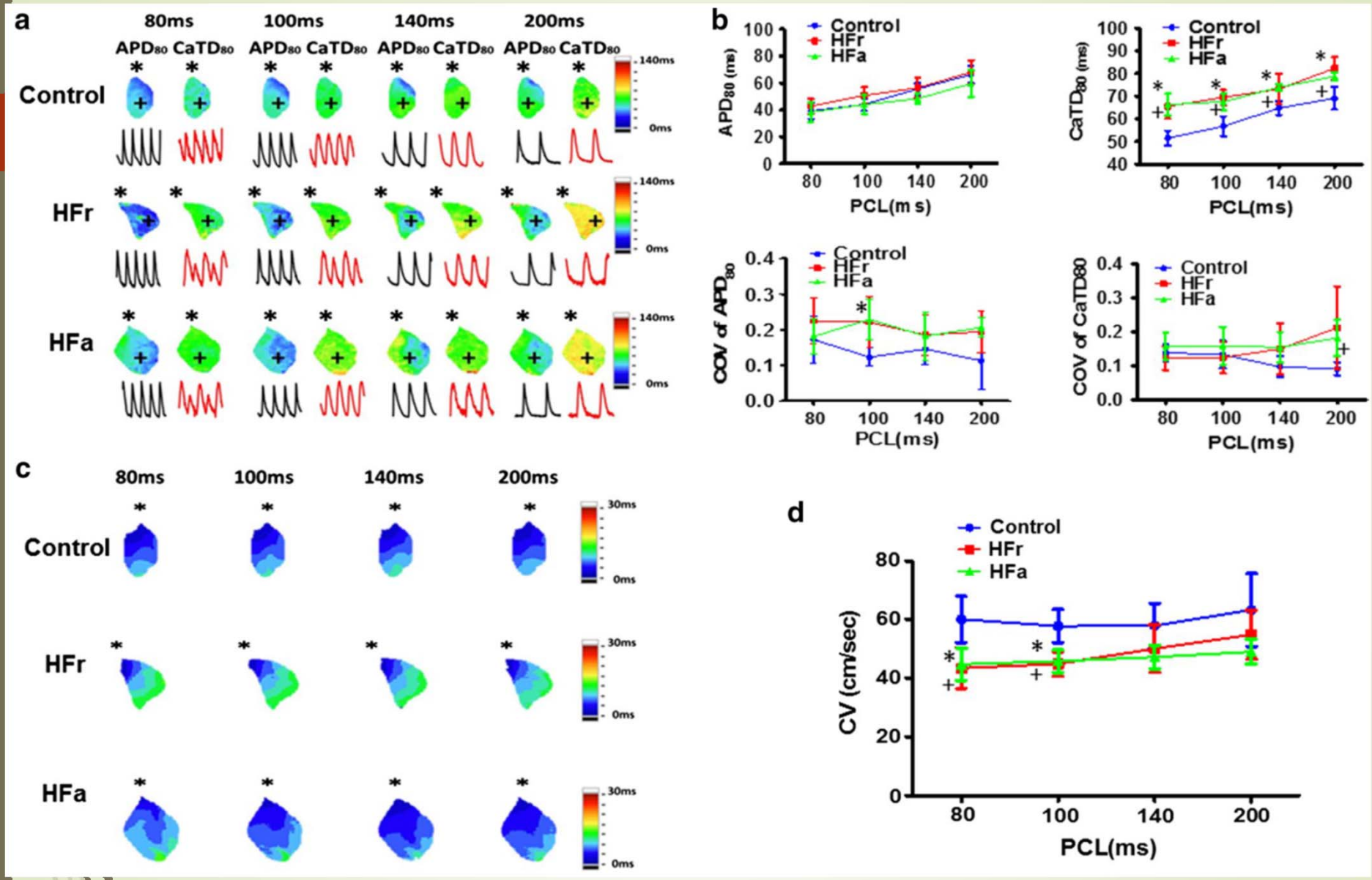

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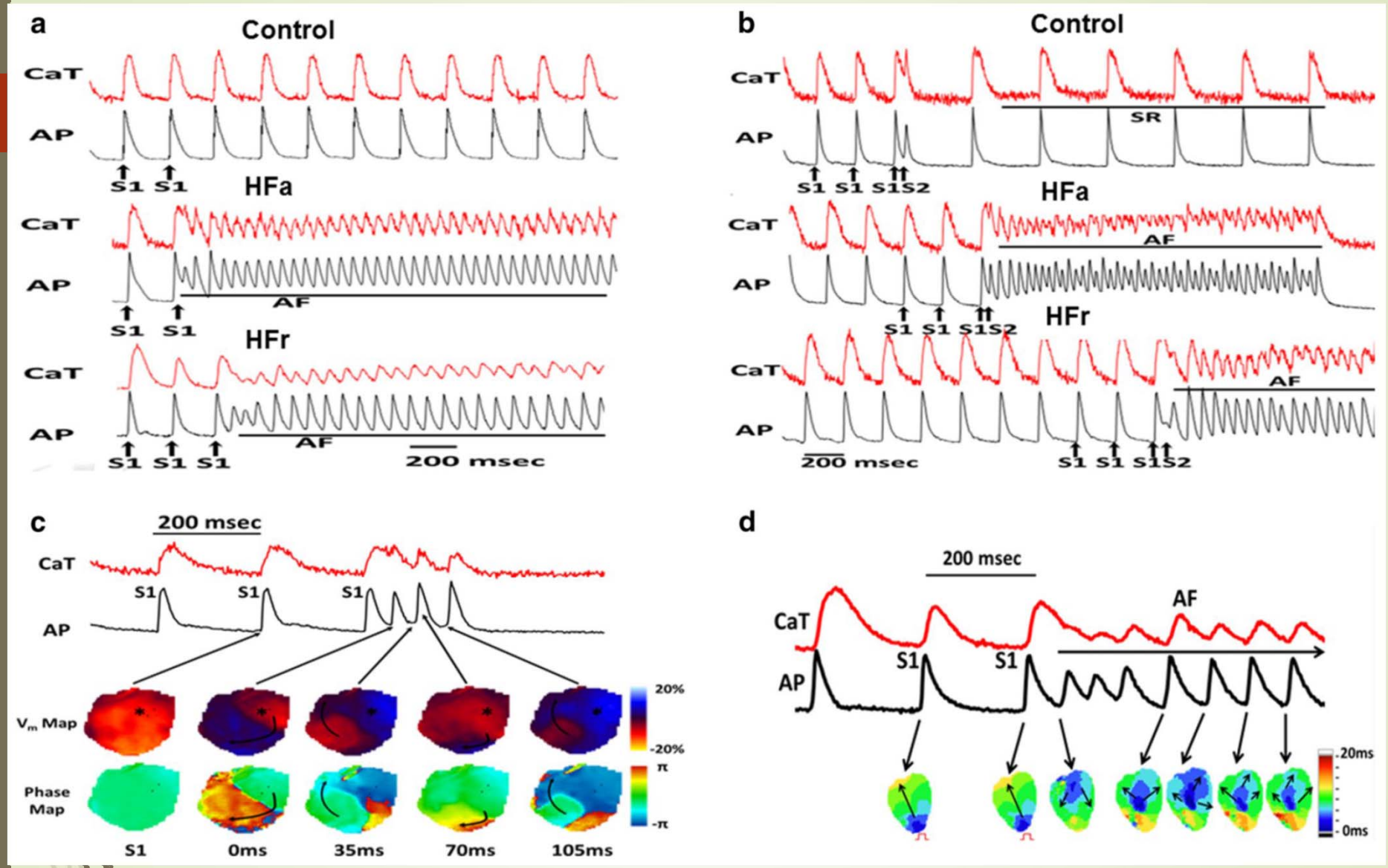

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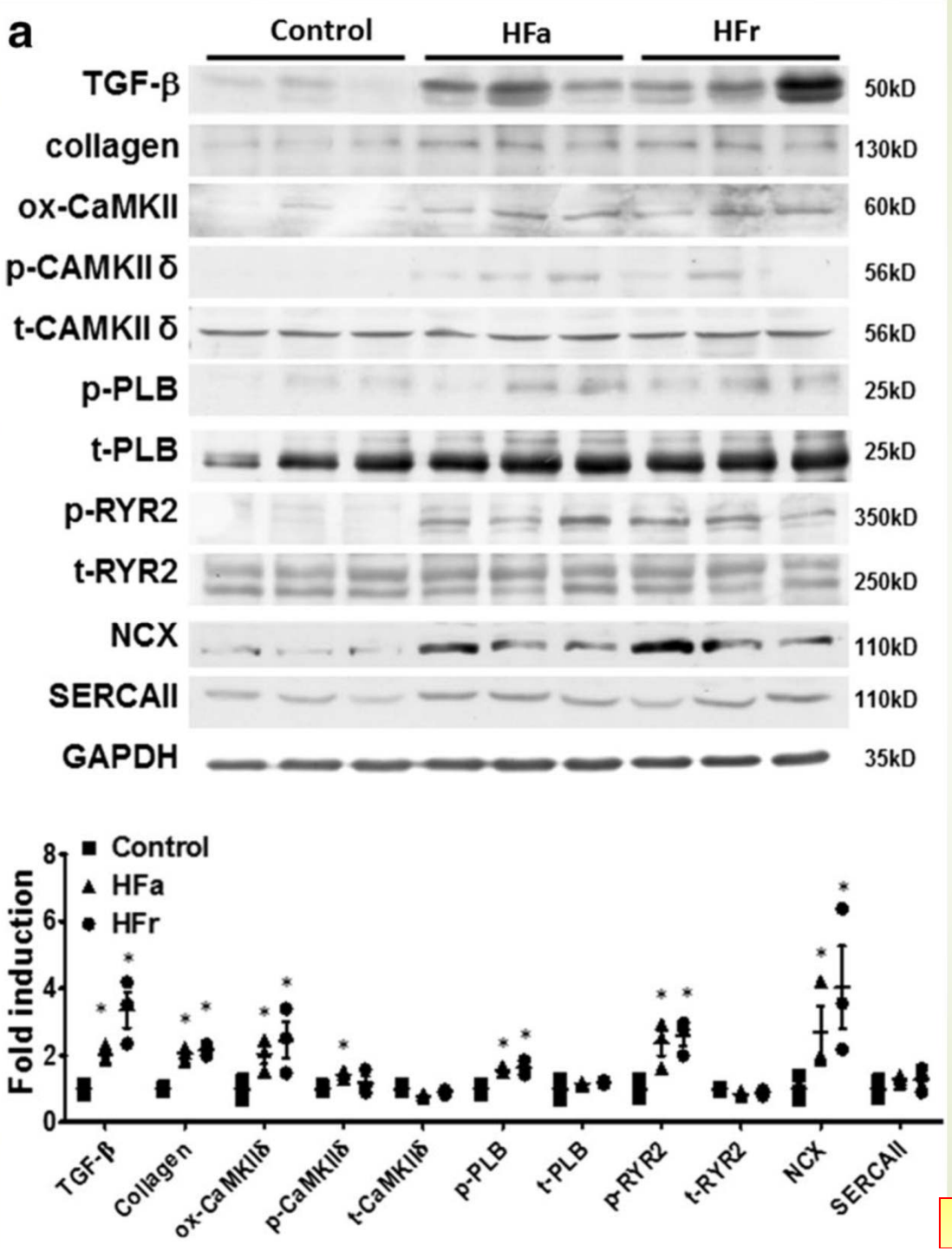

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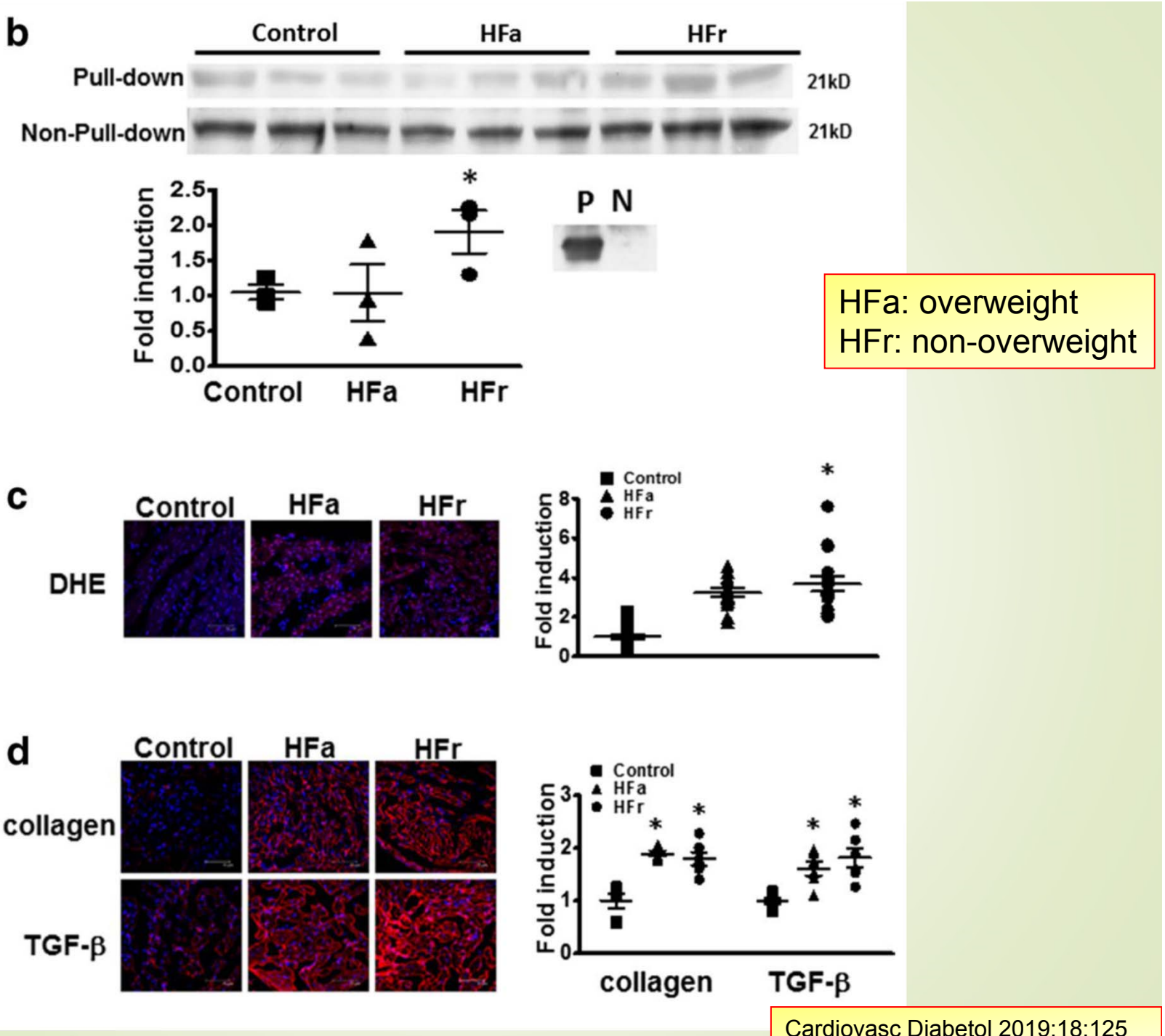

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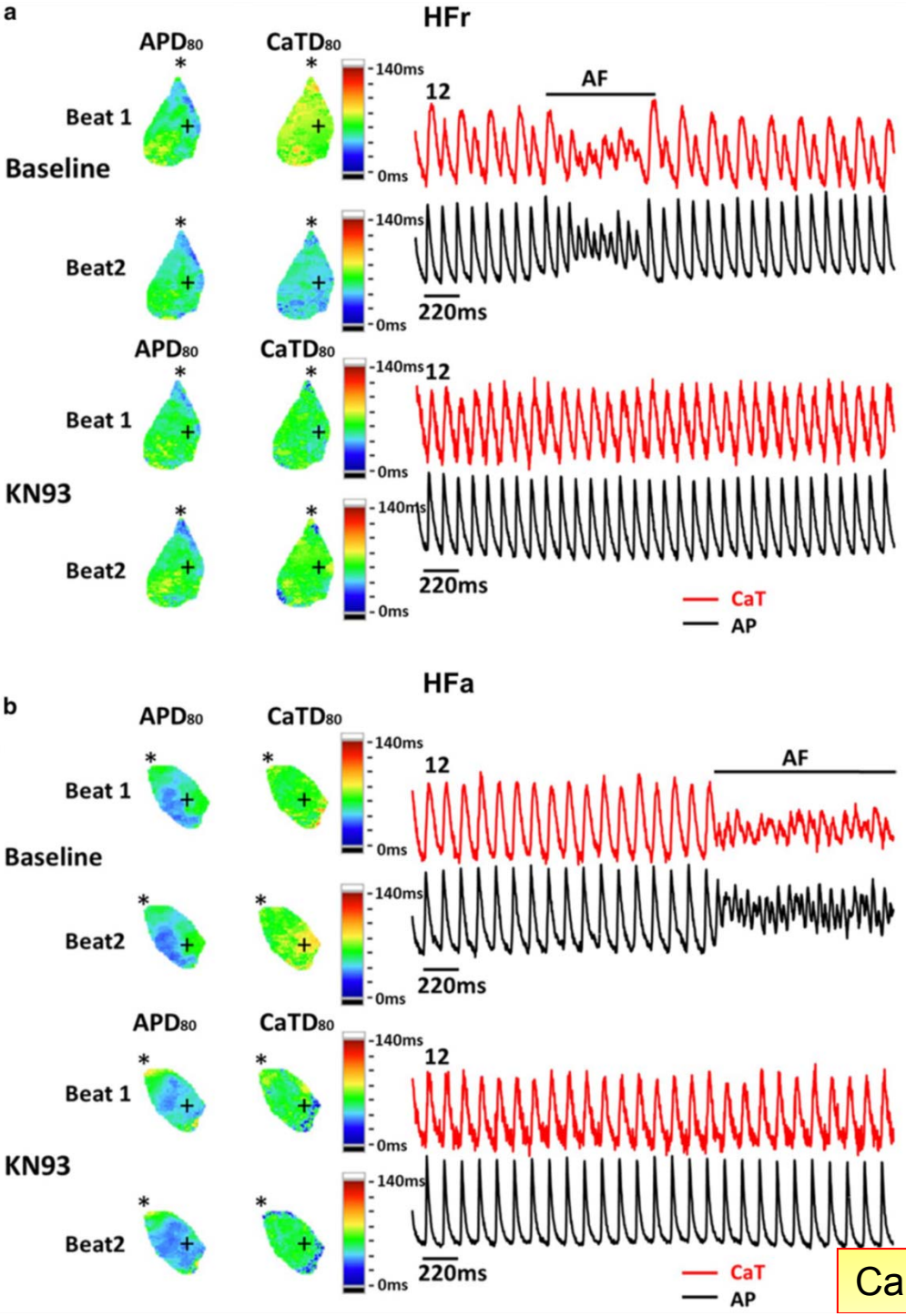

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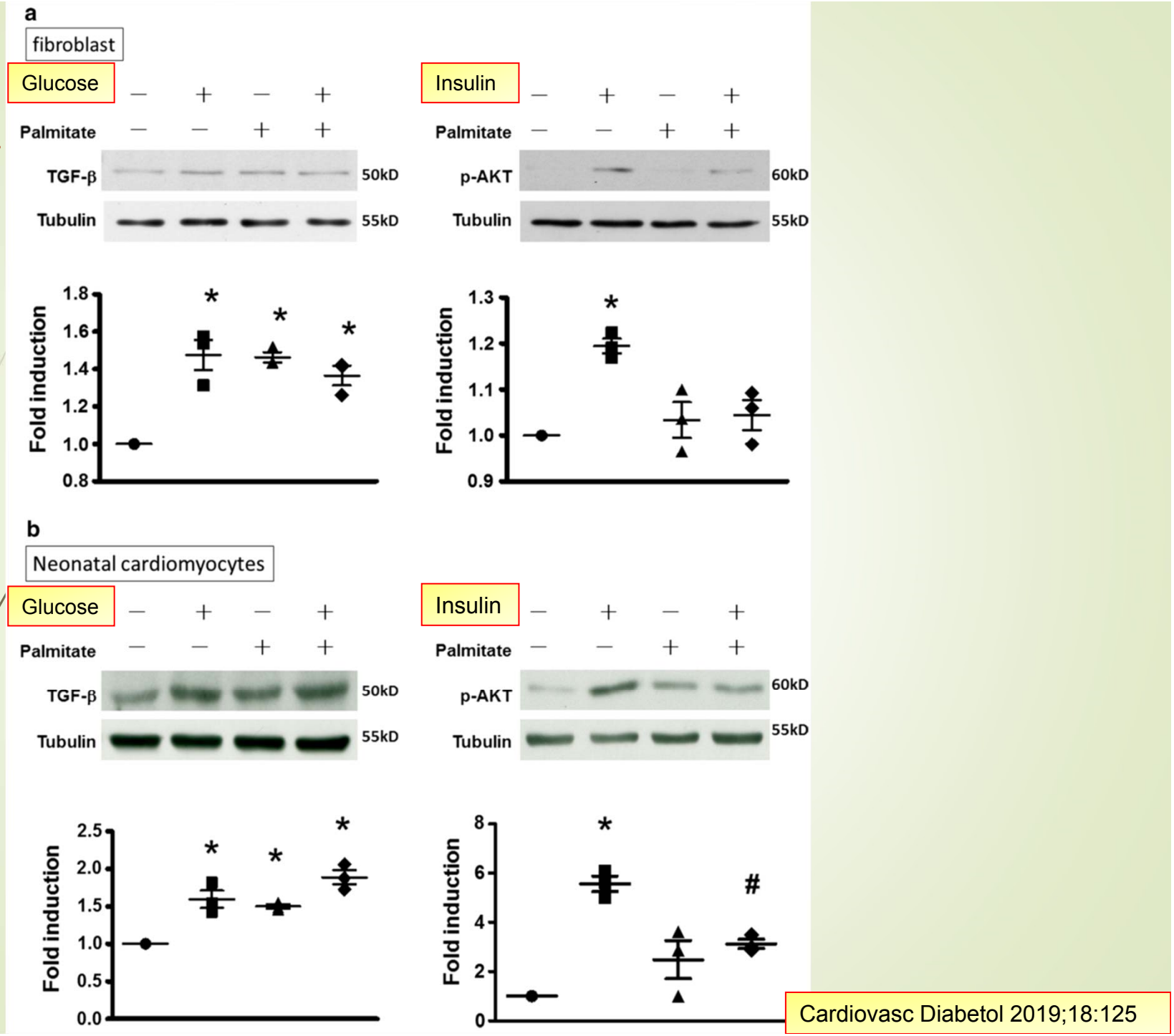

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Conclusion

- Clinical study suggests IR may be an independent factor contributing to AF.
- AF vulnerability are present in both overweight and non-overweight IR rats.
- IR contributes to atrial remodeling, including increased Rac-1-related oxidative stress, dysregulated RyR, intracellular calcium overload, triggered activities in cardiomyocytes and increased TGF-β1 leading to atrial fibrosis.
- Targeting IR, including inhibition of CaMKII, is likely a novel therapeutic intervention in treating and preventing AF.


THANK YOU

SESSION SCHEDULE	
Session Title	Basic 3: Deep Dive in Basic Science for AF
Session Date	(Taiwan Time) June 5 (Sat), 09:15-10:45
Presentation Title	Insulin Resistance and Atrial Fibrillation
Duration	15 min