

# Obstructive sleep apnea associated with Diabetes mellitus Type 2: a proteomic study



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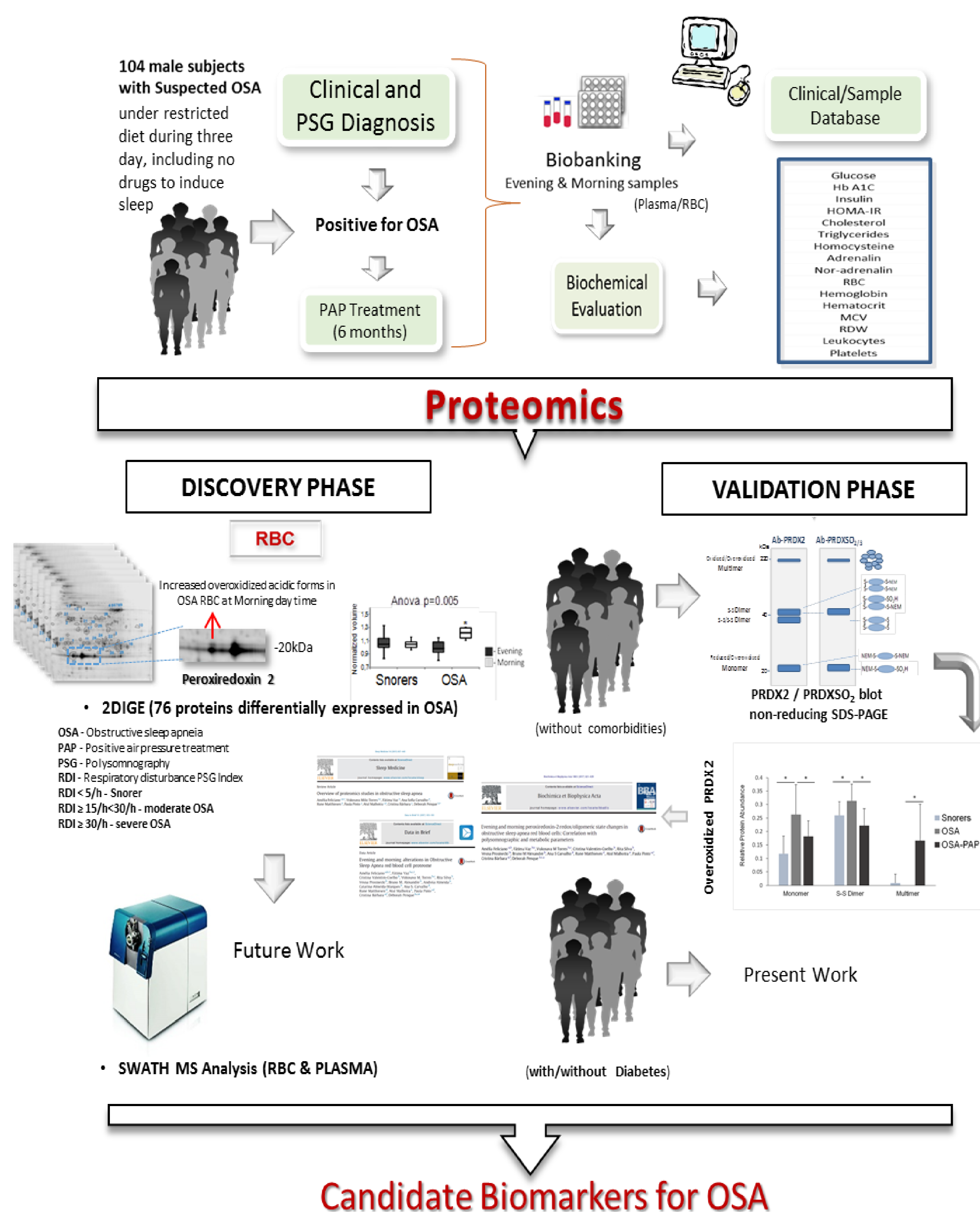
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## INTRODUCTION

We previously showed that Obstructive sleep apnea (OSA), a common public health concern causing deleterious cardiometabolic dysfunction, induces alterations in red blood cell (RBC) proteome, including redox/oligomeric state of PRDX2 as putative biomarker for OSA severity and/or PAP (positive air pressure) therapy monitoring (1-3) (Figure 1). Herein, we aimed to investigate whether OSA patients with Type 2 Diabetes Mellitus before and after positive airway pressure (PAP) treatment present similar changes in the RBC antioxidant protein PRDX2 to better understand the molecular basic mechanisms associated with OSA and OSA outcomes.

Figure 1 Study Workflow



Candidate Biomarkers for OSA

## CONCLUSIONS

The redox/oligomeric state of RBC PRDX2 regulated by overoxidation of the active cysteines were differentially modulated in diabetic OSA patients compared to OSA without this comorbidity. PAP-induced overoxidized oligo forms of PRDX2 associated with chaperone protective function showed decreased in OSA patients with diabetes.

The clinical impact of all these findings needs further investigation and validation.

## METHODS

RBC samples from Snorers (n=22 being 3 diabetics) and OSA patients before and after six month of PAP-treatment (n=29 being 8 diabetics) were analysed by non-reducing western blot using antibody against PRDX2 or PRDXSO<sub>2/3</sub> to measure the total and overoxidized levels of monomeric/dimeric/multimeric forms of PRDX2. Groups were statistically compared and correlated with clinical/biochemical data and significance set up at 5% (p value < 0.05).

## RESULTS

We confirmed our previously data showing higher overoxidation on monomeric forms of PRDX2 in OSA RBC that after PAP treatment decreased followed by an increase of multimeric-overoxidized forms associated with chaperone protective function (Figure 2B, Figure 3B). In contrast, in diabetic OSA RBC, although the level of monomeric PRDX2 was significantly higher abundant compared with OSA RBC without this comorbidity (Figure 2A), its levels of overoxidation was significantly lower (Figure 2B). After PAP treatment, the level of monomeric PRDX2 decreased but not its overoxidation level in diabetic OSA RBC cells (Figure 2A, 2B). The level of oxidized (S-S/S-S) and overoxidized (SO<sub>3</sub>) dimer forms were lower in diabetic OSA RBC compared with OSA RBC without this comorbidity (Figure 2C, 2E). After treatment, the level of overoxidation in these dimers decreased in OSA RBC without comorbidity but not in diabetic OSA RBC (Figure 2E).

Figure 2

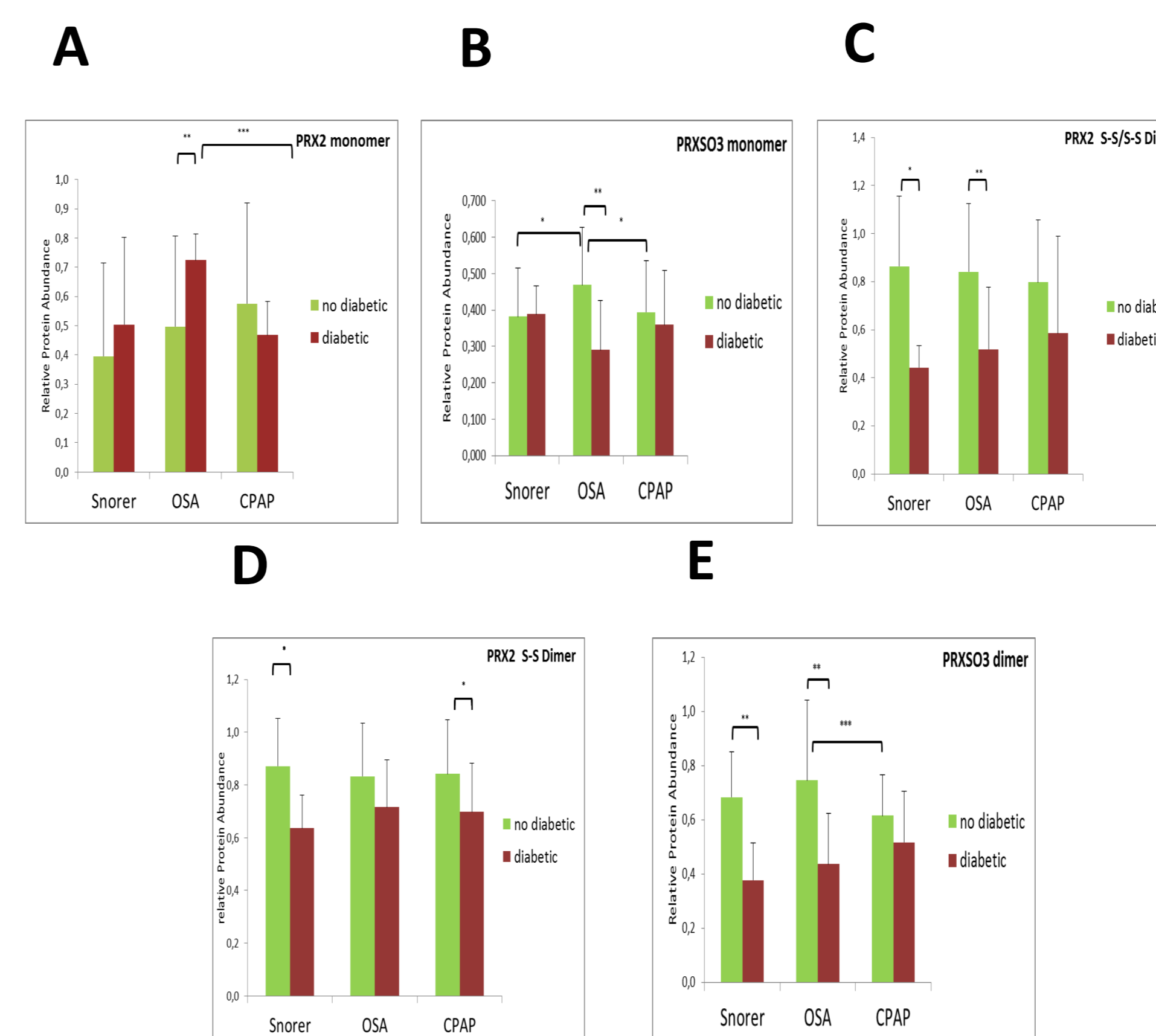
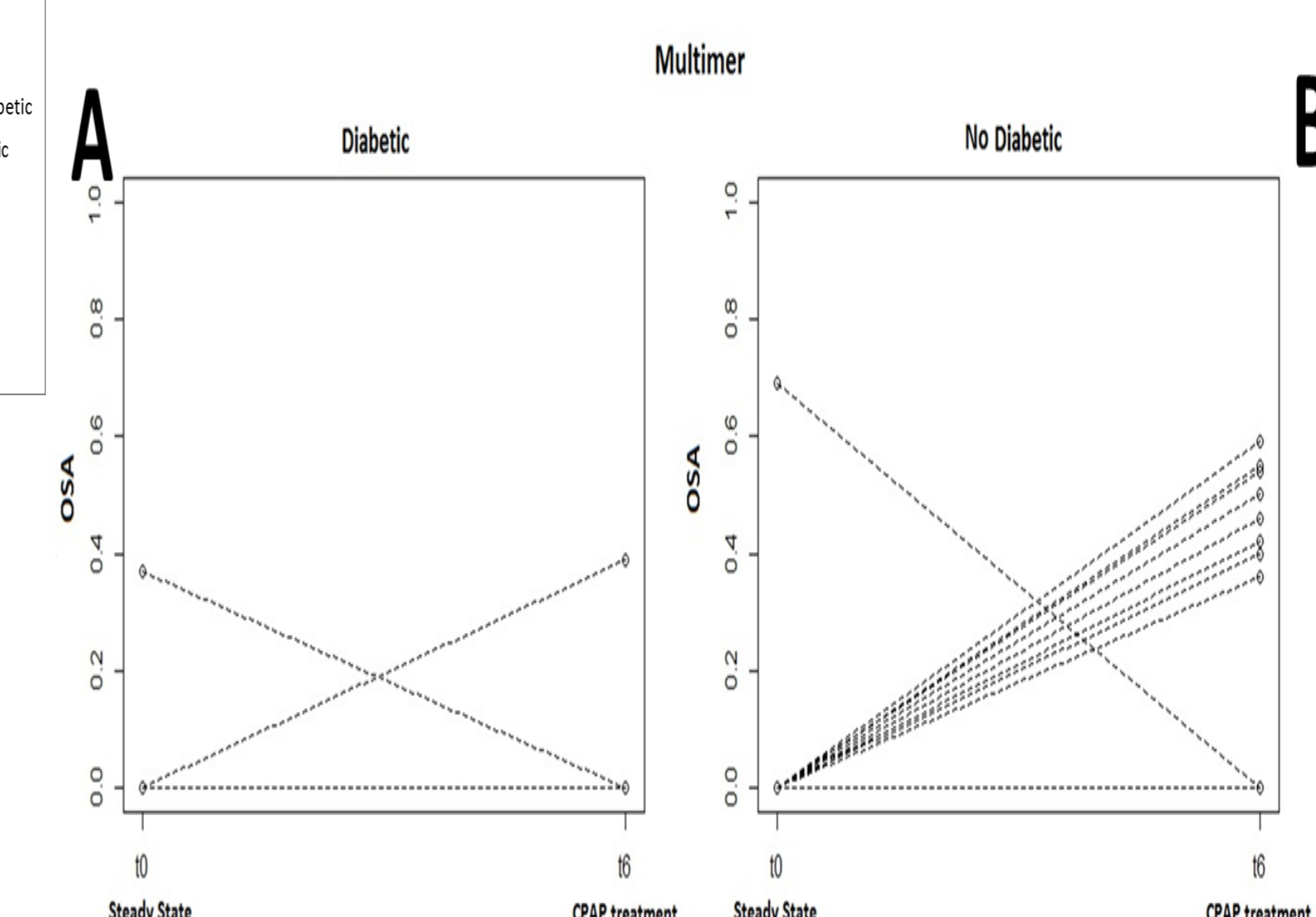


Figure 3



The level of PAP-induced PRDX2-overoxidized-multimers was lower in these diabetic OSA RBC compared with OSA without comorbidity (Figure 3A,3B). The level of overoxidized monomeric/dimeric forms of PRDX2 correlated negatively with levels of insulin / triglycerides and HbA1C, respectively. After PAP, the level of (overoxidized) PRDX2SO<sub>2/3</sub> multimers correlated positively with adrenaline levels (Table)

Correlation of redox/oligomeric state of PRDX2 to biochemical & metabolic variables under study

Table

PRDX2	OSA N=29					PRDX2	OSA N=29					
	Steady State T0	Correlate	Spearman r Value	p Value	Pearson value		p Value	Steady State T6	Correlate	Spearman r Value	p Value	Pearson value
Monomer	Steady State T0	Insulin	(-0,489**)	0,007	(-0,452*)	0,014	Monomer	EPW	—	—	(0,464*)	0,013
		Triglycerides	—	—	(-0,521**)	0,004						
SO <sub>2/3</sub> Monomer	Steady State T0	HbA1C	(-0,456**)	0,028	—	—	S-S Dimer	Triglycerides	(-0,477*)	0,01	—	—
S-S Dimer	Steady State T0	Triglycerides	—	—	(0,449*)	0,015	S-S/SO <sub>2/3</sub> Dimer	Dopamin	(0,418*)	0,027	—	—
SO <sub>2/3</sub> Multimer	Steady State T0	Homocysteine	—	—	(0,467*)	0,011	SO <sub>2/3</sub> Multimer	Adrenalin	(0,670**)	0,00E+00	—	—
		mean cell volume (MCV)	(-0,407*)	0,03	(-0,474**)	0,009						

\*\* Correlation is significant at the 0.01 level (2-tailed).

\* Correlation is significant at the 0.05 level (2-tailed).



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To ICAT-2019 organizers for congress attendance

**References:** (1) Feliciano et al Sleep Medicine 16 (2015) 437–445; (2) Feliciano et al, Biochimica et Biophysica Acta 1863 (2017) 621–629 ; (3) Feliciano et al Data in Brief 11 (2017) 103–110