EVALUATION OF THE IMPACT OF DIABETES MELLITUS ON THE BIOLOGY OF PROSTATE CANCER

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INTRODUCTION AND OBJECTIVES

Prostate cancer (PCa) is a major health concern, being the second most common cancer in men and the sixth most common cause of cancer-related death worldwide. The only established risk factors associated with prostate cancer are age, race and family history. The relationship between the diabetes mellitus and the PCa is still not so well studied. Population studies have shown conflicting results. The aim of our study was to evaluate the impact of diabetes mellitus and glucose levels on the biology of PCa.

MATERIAL AND METHODS

We performed a cross sectional analysis of all patients undergoing radical prostatectomy between January 2009 and December 2016, that included 704 patients who were divided into two groups (diabetic and non-diabetic). We performed an analysis of clinical and histological data seeking to identify the differences on tumor aggressiveness in diabetic and non-diabetic PCa patients. Additionally, our study group performed studies on PCa cell lines (LNCap and PC3) cultured with different glucose levels – normal glucose medium (LG) and a high glucose medium (HG). Proliferation rate, androgen receptor and Her2neu expression and 18F-FDG uptake were determined.

RESULTS

Table 1. Clinical and histological data of diabetic and non-diabetic patients

	Diabetic group	Non-diabetic group	*p*
Number of patients	149	555	
Age (years)	64,5±5,6	62,8±6,7	0.003
PSA preoperative (ng/ml)	9,2±6,3	9,9±12,0	n.s.
Glicemia preoperative (mg/dl)	114,0±25,4	93,9±12,6	0.001
Prostatic volume (cc)	54,2±21,3	47,7±18,1	0.001
Risk groups			
Low-risk	50 (33,6%)	208 (37,5%)	n.s.
Intermediate-risk	80 (53,5%)	261 (47,0%)	
High-risk	17 (11,4%)	63 (11,4%)	
ISUP of RP specimen			
ISUP Grade 1	31 (20,8%)	118 (21,2%)	n.s.
ISUP Grade 2	96 (64,4%)	364 (65,6%)	
ISUP Grade 3	13 (8,7%)	54 (9,7%)	
ISUP Grade 4	3 (2,1%)	12 (2,2%)	
ISUP Grade 5	6 (4,0%)	7 (1,3%)	
Perineural invasion	116 (83,5%)	456 (86,4%)	n.s.
TNM Staging			
pT2	85 (57,0%)	328 (59,1%)	n.s.
pT3	64 (43,0%)	227 (40,9%)	
pN0	93 (62,4%)	357 (64,3%)	
pN1	12 (8,1%)	37 (6,7%)	
pNx	44 29,5%)	161 (29,0%)	
Positive margins	41 (27,5%)	138 (24,9%)	n.s.

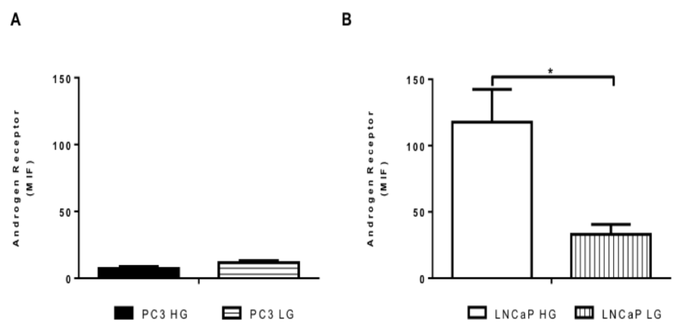

Figure 1 - Expression of androgen receptor in PC3 (A) and LNCaP (B) in high glucose (HG) and low glucose (LG) expressed as mean intensity fluorescence (MIF). We consider a positive staining when MIFs have values higher than 10. For each condition, results were obtained with a minimum of eight experiments. Graphs represent mean±standard error. Statistical significance: *p<0.05.

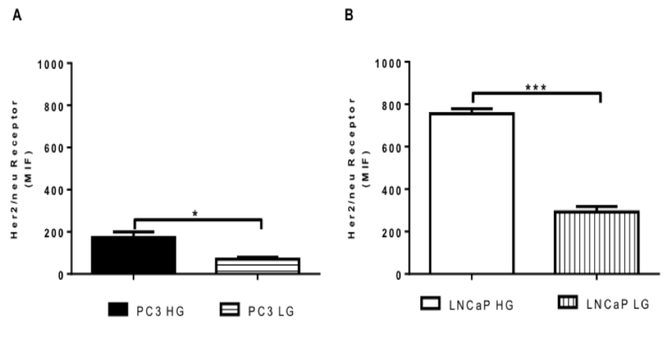

Figure 2 - Expression of Her2/neu receptor in PC3 (A) and LNCaP (B) cell lines in high and low glucose media expressed as mean intensity fluorescence (MIF). Results are expressed as mean±standard error of a minimum of three independent experiments. Statistical significance: *p<0.05; ***p <0.001.

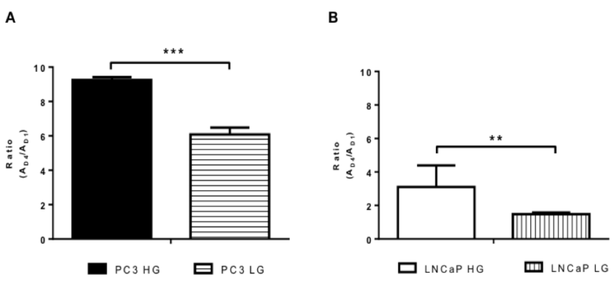

Figure 3 - Results represent the ratio between the measured absorbance after 96h (day 4, A_{04}) and after 24h (day 1, A_{01}) for PC3 (A) and LNCaP (B). Results were obtained with six independent experiments. Values represent mean±SEM. Statistical significance: **p<0.01; ***p <0.001

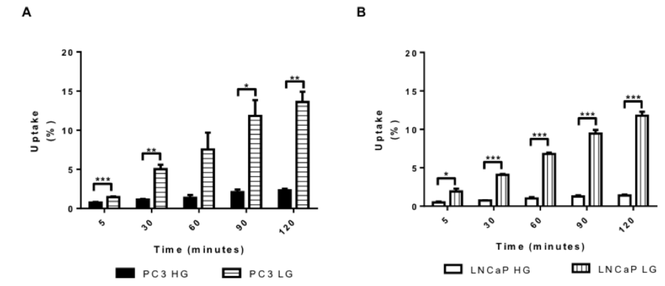

Figure 4 - ^{18}F-FDG uptake in PC3 (A) and LNCaP (B) prostate cancer cells cultures in high and low glucose media, expressed as percentage of uptake. Results are presented as mean±standard error of a minimum of four independent experiments Statistical significance: *p<0.05; **p<0.01; ***p<0.001.

CONCLUSION

Diabetes mellitus and its treatment theoretically can influence PCa by different mechanisms. Our cell lines work attended only to one aspect of the disease, the high glucose level. It was shown that glucose concentration could influence PCa cells behaviour. However, in our patients there was no differences in the oncological variables, despite diabetic patients had bigger prostates.

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