Testosterone Treatment in elderly Hypogonadal Patients does not increase prostate cancer risk: Results of a prospective comparative study. 6 years follow up analysis to Age-Matched Controls

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Objective:
to evaluate the prostate safety parameter including the prevalence and incidence of prostate cancer in elderly hypogonadal subjects under testosterone treatment in comparison with age- and characteristic matched control groups.

Methods: 154 testosterone deficient patients (average age 58 ± 1.7 years and mean follow-up of 42 months, range: 38-61 months), receiving injectable long-acting TU 1000 mg, were compared to a control cohort of 160 eugonadal men (average age 59 ± 2.8 years) with similar characteristics visiting the clinic for preventive medical check up. They underwent monitoring at baseline and 6-monthly including co-morbidities, concomitant medication, International Prostate Symptom Score (IPSS), prostate-specific antigen (PSA), digital rectal examination (DRE), total prostate volume and transitional zone measured by transrectal ultrasound (TRUS). TRUS-guided biopsies were performed when indicated by PSA velocity > 0.75 µg/L, or elevation over 4.0µg/L.

Results: At baseline, hypogonadal patients showed lower PSA values and lower prostate volumes (0.68 ± 0.4 µg/L and 25.6 ± 1.4 ml, respectively). Subjects in the control group had PSA levels of 2.42 ± 1.2 µg /L, and prostate volume 38.4 ± 2.42 ml at baseline. Hypogonadal patients whose PSA velocity in the observation period was > 0,75 µg /L, underwent TRUS-guided prostate biopsies (10 cores 2.2 cm each or saturating biopsies 24-32 cores 2.2 cm each in those men for whom a repeat biopsy was indicated). We found CaP in 5/22 biopsies, three of them unilateral with up to 10% tumor cells in a core. Gleason scores were 3+2 or 3+3. Two patients had a high grade prostate intra-epithelial neoplasia (PIN). In the 160 control subjects, 16/39 subjects who underwent biopsies showed CaP, 14 of them bilateral,with a significantly higher Gleason score of 3+3 till 4+5 and up to 80% tumor cells in a core. No subject of both groups showed any abnormality in rectal palpation.

Conclusions:
Subjects with T-deficiency have lower prostate volumes and PSA levels than eugonadal ones. Testosterone therapy does not increase CaP incidence. The group on testosterone treatment had smaller tumors and less malignancy (better differentiation). Hypogonadism offers no protection against the development of biopsy-detectable prostate cancer. Lower levels of total testosterone or free testosterone were associated with an increased risk of cancer. Hypogonadal patients untreated with TRT could be at higher risk to have bigger and more aggressive prostate cancers.

Table 1 (6 years)
Pathological Results of Biopsies

	Group I, N= 154 (hypogonadal and ED)	*Group II, N= 160 (control)*
Number of biopsies	**22**	**39**
Prostate cancer	**5**	**16**
Unilateral	**3**	**2**
Bilateral	**2**	**14**
% tumor cells	**10**	**up to 80**
Gleason score	**3+2 / 3+3**	**3+3 to 5+4**
others	**2 high-grade PIN**	**7**

Table 2 (6 years) 5/154 CaP Cases
Post-Surgical Outcomes TRT Group

	Group I, N= 154 (hypogonadal/ED TRT=TU 1000mg im)				
Patient no.	***1***	***2***	***3***	***4***	***5***
PSA	2.91	2.44	2,34	1,99	3,17
Tumor stage	**pT2a**	**pT2a**	**pT2c**	**pT2b**	**pT2a**
Grading	**GII**	**GII**	**GII**	**GII**	**GII**
Gleason score	**3+3**	**3+2**	**2+3**	**3+3**	**3+3**
Lymph nodes	0	0	0	0	0
Surgical margin	neg	neg	neg	neg	neg
Bone metastases	0	0	0	0	0

Table 3/ I (6 years) 16/160 CaP Cases
Post-Surgical Outcomes Control Group

	Group II (control), N= 160						
Patient no.	***1***	***2***	***3***	***4***	***5***	***6***	***7***
PSA	8,06	3.75	3.2	10.6	4.79	5.42	3.79
Tumor stage	**pT3b**	**pT2c**	**pT2c**	**pT2c**	**pT3a**	**pT3a**	**pT2c**
Grading	**GIII**	**GII**	**GIII**	**GIII**	**GIII**	**GIII**	**GIII**
Gleason score	**4+3**	**3+3**	**3+4**	**3+4**	**3+4**	**4+4**	**3+4**
Lymph nodes	0	0	0	0	0	+	0
Surgical margin	**pos**	neg	neg	neg	**pos**	neg	neg
Bone metastases	0	0	0	0	0	0	0

Table 3/ II (6 years) 16/160 CaP Cases
Post-Surgical Outcomes Control Group

	Group II (control), N= 160						
	8	***9***	***10***	***11***	***12***	***13***	***14***
PSA	5,34	3,23	10,44	8.66	4.99	9,6	6,15
Tumor stage	**pT3b**	**pT2c**	**pT3c**	**pT3b**	**pT2c**	**pT3b**	**pT3a**
Grading	**GIII**	**GII**	**GIII**	**GIII**	**GII**	**GII**	**GIII**
Gleason score	**4+3**	**3+3**	**5+4**	**3+4**	**3+3**	**3+4**	**3+4**
Lymph nodes	0	0	+	0	0	0	0
Surgical margin	pos	neg	pos	neg	neg	neg	pos
Bone metastases	0	0	0	0	0	0	0

Table 3/ III (6 years) 16/160 CaP Cases
Post-Surgical Outcomes Control Group

	Group II (control), N= 160	
Patient no.	***15***	***16***
	2,42	
Tumor stage	**pT2c**	**pT2c**
	GII	**GII**
Gleason score	**3+3**	**3+3**
Lymph nodes	0	0
Surgical margin	neg	neg
Bone metastases	0	0