Original Article

Investigation into a possible association between telomere length in prostate cancer patients and non-prostate cancer patients

Karuha Martwachira[1], Navakun Kaewtunjai[2], Wirote Tuntiwechapikul[2], Bannakij Lojanapiwat[1]

[1]Division of Urology, Department of Surgery, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand
[2]Department of Biochemistry, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand

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Abstract

Objective: The objective of this study was to investigate a possible association between leukocyte telomere length (LTL) in prostate cancer patients and non-prostate cancer patients.

Material and Method: Enrollment criteria for the study were: patients over 50 years of age who were being screened for prostate cancer or had an abnormal digital rectal examination and whose serum PSA was higher than 4 ng/dL or had increased more than 0.75 ng/dL per year.

Clinical data and laboratory data were recorded and participants were divided into 2 groups: a prostatic cancer patient group and a non-prostatic cancer group, as dictated by the pathological findings. We compared the leukocyte telomere length in each group. Primary outcome was the LTL in the prostatic group and the non-prostatic group. The secondary outcome was what affected the LTL in prostate cancer patients. Univariable and multiple linear regression analytical outcomes were compared. A p-value <0.05 was deemed to be statistically significant.

Result: Two hundred patients were included in the study: 87 in the prostatic cancer group and 113 in the non-prostatic cancer group. Baseline characteristics of participants are summarized. The mean age of the cancer patients was 70.09 years and 67.61 years in non-cancer group.

The mean LTL was 5.37 in the prostatic cancer group and 5.40 in the non-prostatic cancer group (p=0.736). The mean serum PSA was significantly higher in the prostatic cancer group compared with the non-prostatic cancer group (307.76 vs 11.80, respectively) (p<0.001). This analysis showed that older age (60 years plus) was significantly associated with shorter leukocyte telomere length (p=0.01). However, other factors were not associated with leukocyte telomere length.

Conclusion: In this prospective study, leukocyte telomere length was not significantly different between the prostatic cancer group and the non-prostatic cancer group. Aging (60 years old plus) and distant organ metastasis were significantly associated with leukocyte telomere length.

Corresponding author: Bannakij Lojanapiwat
Address: Faculty of Medicine, Chiang Mai, University, 110, Inthavaroros Rd, Si Phum, Muang, Chiang Mai, 50200, Thailand.
E-mail: dr.bannakij@gmail.com

Introduction

To date, aging is acknowledged as an important risk factor in the development of disease. Malignancy, degenerative diseases, metabolic syndrome and cardiovascular disease are all associated with increased age. Although aging may be an influential risk factor for disease, there is an insufficiency of data to explain the exact biological mechanisms involved.

Telomeres are key structures at either end of each chromosome. The decrease in the length of the telomeres is known to be a marker of biological aging. In newborns, the length of telomeres is approximately 8,000; this number will have decreased to 1,500 base pairs by old age[11]. Shortening of the telomere length at each cell division results in increasing carcinogenesis[1]. The telomere lengths of prostatic cancer cells are shorter than in normal prostatic cells[2]. Shortened leukocyte telomere length has been shown to be related to cancer development in the bladder, lungs and kidneys[4,5]. In addition to the carcinogenic impact, the presence of other metabolic and cardiovascular diseases are associated with telomere length[6-9].

In this study, we aimed to study the association between leukocyte telomere length (LTL) in prostate and non-prostate cancer patients.

Material and Method

This was a prospective study which recruited participants from the Urology Outpatient Clinic in the Department of Surgery, Chiang Mai University Hospital. The study protocol was approved by the Research Ethics Committee, Faculty of Medicine, Chiang Mai University (STUDY CODE: SUR-2559-03758). Inclusion criteria were patients aged more than 50 years who underwent screening for prostate cancer with an abnormal digital rectal examinationand whose serum PSA was higher than 4 ng/dL or had increased more than 0.75 ng/dL per year. The patients who refused to participate in the study were not included. All participants gave their written informed consent before enrollment.

Clinical data including age, weight, height, waist circumference, underlying disease and current medication were collected. The laboratory data including serum PSA, fasting blood glucose, LDL, HDL, and triglyceride levels were all recorded. A biopsy was performed in all cases; leukocyte telomere length was ascertained using the monochromatic multiplex real-time quantitative technique and a prostatic pathology report was recorded. The prostatic biopsy pathology report was used to divide the patients into 2 groups: the prostatic and non-prostatic cancer groups.

We compared the leukocyte telomere lengths in each group. The primary outcome was the leukocyte telomere length in the 2 groups. The secondary outcome was the factors that affect the leukocyte telomere length in the prostate cancer group. Univariable and multiple linear regression analyses were carried out. Statistical significance was taken as a p-value <0.05.

Result

Two hundred patients were recruited onto the study. Eighty-seven patients were in the prostatic cancer group and 113 patients in the non-prostatic cancer group. Baseline characteristics of the patients are reported in Table 1. The mean age in the prostatic cancer group was 70.09 years. The mean age of the non-prostatic cancer group was 67.61 years old.

There was a trend for the mean leukocyte telomere length to be shorter in the prostatic cancer group, but the difference was not statistically significant (5.37 VS 5.40, respectively, p=0.736).

The univariable analysis in the prostate cancer group showed that older age (60 years old plus) was significantly associated with leukocyte length (p=0.011). In the same way, age greater than 70 years was related significantly to LTL (p<0.001). In addition, distant organ metastasis from prostate cancer (lung/bone)was also associated with LTL (p=0.021). However, other factors tested (serum PSA, stage of

cancer, UCSF CAPRA risk score, BMI, prostate cancer, smoking, Gleason grade group, metabolic syndrome and metastatic cancer) were not associated with leukocyte telomere length (Table 2).

From multiple linear regression analysis, aging (more than 70 years) and prostate cancer metastasis (lung/bone) were associated with LTL ($p<0.001$, $P=0.18$ respectively) (Table 3).

Table 1. Baseline characteristrics of participants.

Parameters	Cancer (N=87)	No Cancer (N=113)	p-value
Age, Year			
< 55	2 (2.30)	5 (4.42)	0.380
55-70	45 (51.72)	67 (59.29)	
> 70	40 (45.98)	41 (36.28)	
Mean (SD)	70.09 (8.63)	67.61 (7.55)	
BMI			
Mean (SD)	23.65 (5.25)	23.55 (3.32)	0.875
HDL			
Mean (SD)	50.08 (15.57)	54.21 (16.45)	0.082
Triglyceride			
Mean (SD)	123.25 (49.86)	116.92 (81.47)	0.536
FBS			
Mean (SD)	98.30 (20.80)	99.85 (26.93)	0.666
SBP			
Mean (SD)	132.63 (19.19)	133.04 (16.17)	0.872
DBP			
Mean (SD)	74.69 (12.22)	78.10 (11.00)	0.045
Smoking, n (%)			
< 15 pack year	22 (26.51)	17 (16.04)	0.103
≥ 15 pack year	61 (73.49)	89 (83.96)	
Prostate Volume			
Mean (SD)	45.08 (26.47)	54.73 (70)	0.020
Telomere length			
Mean (SD)	5.37 (0.72)	5.40 (0.50)	0.736

Table 2. Univariable logistic regression of telomere length.

Parameters	Odd Ratio	95 % CI for odds		p-value
		Lower	Upper	
Age				
> 60	0.635	0.008	0.528	0.011
Age				
> 70	0.155	0.059	0.410	< 0.001
Clinical T stage				
Stage 2	1.167	0.197	6.893	0.865
Stage 3	0.567	0.103	3.125	0.514
Stage 4	0.400	0.040	3.955	0.433
GS	0.792	0.546	1.149	0.219
UCSF-CAPRA				
Low	Reference	-	-	-
Intermediate	0.611	0.047	7.882	0.706
High	0.295	0.025	3.435	0.330
Grade Group				
Grade 2	0.938	0.114	7.728	0.952
Grade 3	0.486	0.109	2.160	0.343
Grade 4	0.221	0.052	0.944	0.042
Grade 5	0.469	0.122	1.799	0.269
Metabolic syndromes				
No	1.010	0.413	2.470	0.982
Smoking label				
≥ 15	1.273	0.478	3.390	0.629
Metastasis (Bone/Lung)	0.324	0.124	0.846	0.021
PSA	1.000	0.999	1.001	0.989

Table 3. Multiple linear regression of telomere length.

Parameters	Odd Ratio	95 % CI for odds		p-value
		Lower	Upper	
Age (> 70)	0.140	0.050	0.389	< 0.001
Metastasis (Bone/Lung)	0.275	0.095	0.798	0.018

Discussion

In this prospective study, we found that shorter circulating leukocyte telomere length may possibly be associated with prostate cancer. However, the results were not significant.A larger sample size in a future study may give weight to this finding. In addition, we found that the only factor that was significantly associated with leukocyte telomere length is old age.

One prior prospective study indicated that shorter telomeres tended to be associated with a lower risk of prostate cancer[13]. This study also indicated that other factors can affect the length of telomeres, such as age, metabolic syndrome, and heavy smoking. Two other prospective studies reported that longer telomere length was associated with an increased cancer risk[10-12]. These studies showed that telomere length between prostate cancer patients and non-prostate cancer patients were not significantly different, the same as our findings.

The strengths of this study include its prospective design and detailed clinical information on the grade and stage of the cases. However, this study also had some limitations. We had a small number of patients compared with prior studies, which could explain why not all our results showed a correlation with previous studies. The ages between the 2 groups of patients in our study differed significantly (70.09 vs 67.01) (p=0.031). Our results did not indicate any major differences in the association between subtypes.

Conclusion

In this prospective study, leukocyte telomere length was not significantly different in the prostatic cancer group compared with the non-prostatic cancer group. Both aging and distant organ metastasis prostate cancers were significantly associated with leukocyte telomere length. Future large, prospective, longitudinal studies are needed to confirm these findings. A full understanding of leukocyte telomere length epidemiology and prostate cancer association will facilitate intervention efforts to prevent cancer and improve the lives of patients through the modulation of telomere dynamics.

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Conflict of interest

The authors declare no conflict of interest.

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