

Influence of *IL-6* and *IL-1β* Gene Polymorphisms on Clinical and Morphological Characteristics of Cervical Tumors and Patient Survival

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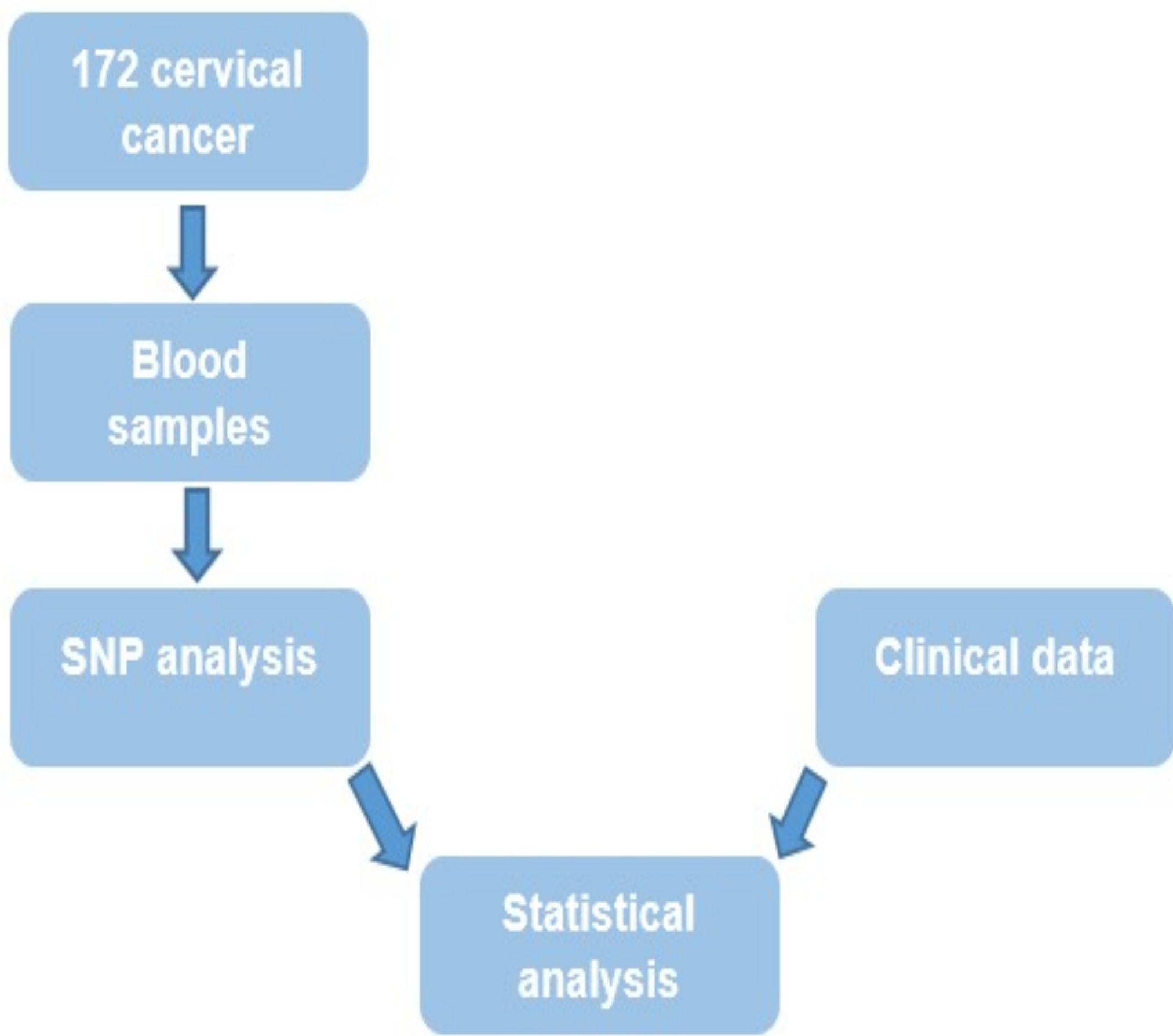
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Objective

Cervical cancer is 4th most common cancer in women worldwide. The main causative factor of this disease is human papilloma virus (HPV). In developed countries, where regular checkups, vaccination programs and various other preventative measures are a standard of care, the rate of cervical cancer was reduced by half in the last 30 years. Despite that, the disease still remains a significant issue. It is known that chronic inflammation has an important role in carcinogenesis processes. *IL-6* and *IL-1β* are important cytokines partaking major roles in inflammatory process. Studies show a significant correlation between polymorphisms in *IL-6* and *IL-1β* genes and increased risk of various cancers. Objective of this study was to evaluate 4 polymorphism (*IL-6* gene rs1800795 and rs1800797, *IL-1β* gene rs1143634 and rs16944) genotype and allele frequencies and their correlation with clinical and morphological cervical tumor characteristics and survival in Lithuanian cervical cancer patient group.

Methods

- A total of 172 patients (mean age 55 years) with cervical cancer diagnosis were enrolled in the study, which was approved by Kaunas Regional Biomedical Research Ethical Committee (BE-210 and BE-2-10/2014).
- DNA for SNP analysis was extracted from peripheral blood leukocytes. Real Time-PCR (RT-PCR) method was used for SNP analysis. All clinical and morphological patient data was obtained from medical records by oncologists in Lithuanian University of Health Sciences Kaunas Clinics. Every participant signed informed consent forms.
- Study data included age at diagnosis, tumor staging based on TNM and FIGO classification, histological type, tumor grade (G1 and G2, G3), progress and death. Associations between SNPs and patient clinical characteristics and disease outcome were evaluated. Statistical analysis was performed using SPSS program.



Results

- rs1800797 polymorphism of *IL-6* gene was associated with disease progress to local lymph nodes. Our data indicated that GG genotype carriers, compared to AA genotype carriers, had 3.24 times higher probability of developing metastases to local lymph nodes (OR 3.243 CI 1.378-7.583, p=0.007);
- A borderline significant link between *IL-1β* rs16944 polymorphism G allele and overall survival (OR 0.386 CI 0.148-1.007, p=0.052) was found;
- rs1800795 polymorphism of *IL-6* gene and rs1143634 of *IL-1β* had no significant correlations with tumor clinical and morphological characteristics.

Table 1. Clinicopathological characteristics of the study group.

Characteristics	Subgroups and frequencies
Age at diagnosis	<50 - 26%; ≥50 - 74%
Histological type	squamous cell carcinoma - 94,2%; other - 5,8%
TNM stage	T1 + T2 - 63,4%; T3 + T4 - 36,6%
FIGO stage	I + II - 43,6%; III + IV - 56,4%
Tumor grade	G1 + G2 - 72,7%; G3 - 27,3%
Lymph node status	normal - 55,2%; affected - 44,8%
Metastasis	absent - 94,2%; present - 5,8%
Progress	absent - 71,5%; present - 28,5%
Death	no - 76,7%; yes - 23,3%

T1, T2, T3, T4 – tumor staging according to TNM classification; I, II, III, IV – tumor staging according to FIGO classification, G1 – well differentiated; G2 – moderately differentiated; G3 – poorly differentiated..

Table 2. Polymorphism genotype and allele distribution and frequency.

Gene	Polymorphism	Genotype distribution (frequency)	Allele distribution (frequency)
<i>IL-1β</i>	rs1143634	CC – 107 (0,622)	C – 0,79 T – 0,21
		CT – 58 (0,337)	
		TT – 7 (0,041)	
<i>IL-1β</i>	rs16944	GG – 65 (0,387)	G – 0,65 A – 0,35
		GA – 93 (0,541)	
		AA – 14 (0,081)	
<i>IL-6</i>	rs1800795	CC – 51 (0,297)	C – 0,54 G – 0,46
		CG – 84 (0,488)	
		GG – 37 (0,215)	
<i>IL-6</i>	rs1800797	AA – 48 (0,279)	A – 0,53 G – 0,47
		AG – 86 (0,500)	
		GG – 38 (0,221)	

Conclusions

Our study suggests that there is a correlation between *IL-6* and *IL-1β* gene polymorphisms and cervical cancer morphology. However, to confirm the significant correlations, a bigger study with more participants is required.

Key words

Cervical cancer; *IL-6*, *IL-1β*, SNP.