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Journal of Urology and Research

Short Communication

On Joint Analysis of Testicular Germ Cell Cancer

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Abstract

A joint semi-parametric statistical analysis of height and weight case-control data show that jointly these two variables are significant risk factors for testicular germ cell tumors. However, body mass index, which is a function of height and weight, is a not a significant risk factor.

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Submitted: 19 September 2017

Accepted: 18 January 2018

Published: 25 January 2018

ISSN: 2379-951X

Keywords
- Case-control
- Exponential tilt
- Reference distribution
- Density ratio model
- Testicular cancer

INTRODUCTION

Testicular germ cell tumor (TGCT) is a rare type of cancer which a icts men mainly in the age group 15-44 years. It is more likely among men of northern European ancestry than among men of Asian, Middle Eastern, and African descent [1,2,3]. It is noted in [4] that an increase in testicular cancer incidence have been observed during the second half of the last century mainly in countries attaining high levels of human development. Notwithstanding an apparent attenuation in the last decade, rates continue to increase in developing countries.

Well known risk factors are cryptorchidism, prior history of TGCT, and family history of TGCT [5]. Men with seminoma, history of TGCT, or family history of TGCT have a higher rate of TGCT. Other possible risk factors include body size, dairy consumption, and age at puberty [6,7].

In [7], using the odds ratio as a criterion, it has been shown that body size as expressed by increased height is a significant TGCT risk factor. On the other hand, body mass index which is a function of both height and weight (weight in kilograms divided by height in meters squared) was not found to be a risk factor.

The question is whether height and weight jointly are risk factors, a problem that can be approached by estimating, semi-parametrically, their joint bivariate probability distribution. This has been considered in [8]. The present paper is a review of the method and results from that work.

Specically, we analyze the data in [7] in testing equidistribution between the case and control groups by applying a likelihood ratio test obtained from semi-parametric considerations. That is, testing for a similar bivariate statistical behavior in the case and control groups by estimating the joint two-dimensional height-weight distributions in both groups. Such a bivariate analysis leads to results which cannot be obtained from marginal considerations alone, or even from logistic regression analysis with height and weight modeled together.

ANALYSIS OF TESTICULAR GERM CELL DATA

The TGCT data used here consist of pairs of heights (cm) and weights (kg) of 1691 individuals, of which $n_1 = 928$ are cases and $n_2 = 763$ are in the control group. In each group the data are (x; y) = (hight; weight) pairs, where the control density (the so called reference density) is g(x; y) and the case density is $g_1(x; y)$.

The following density ratio model has been found appropriate [8,9],

$$g_1(x; y) = \exp(\ + \ _1x + \ _2y)g(x; y) \qquad (1)$$

and the hypothesis of interest is $H_0 : \ _1 = \ _2 = 0$. This is so since $_1 = \ _2 = 0$ implies that = 0 as well, in which case $g_1 = g$, meaning bivariate equi-distribution. Different variants of model (1), including a Bayesian version and quite a few applications, have been discussed in detail in [10] and in the recent book [11].

Maximum likelihood estimates of the parameters obtained from the fused case-control data are

$$(\hat{}; \ _1; \ _2) = (4{:}676; \ 0{:}025; \ 0{:}002) \qquad (2)$$

with respective standard errors (0:914; 0:006; 0:004). Based on these esti-mates, the likelihood ratio test of H_0 gives a p-value of 0:0005, indicating very different statistical behavior in the two groups. Hence, height and weight jointly are significant TGCT risk factors.

A univariate formulation of the density ratio model regarding height only gives (by fusing the case-control height data) a p-value of 0.00011 which indicates that height alone is a TGCT risk factor. On the other hand, a univariate formulation of the density ratio model regarding body mass index gives a relatively high p-value of 0.88213, indicating that body mass index is not a risk factor, echoing the univariate results in [7] obtained from logistic regression analysis.

CLOSING REMARKS

The previous analysis demonstrates the power of fusing data from many sources. This gives both univariate and multivariate distributions used in discovering risk factors.

Other urological problems can benefit from the semi-parametric approach outlined in this paper. For example, a certain extension of the semi-parametric method has been applied in the estimation of the small tail probability that an observed PSA level exceeds a very high threshold, using moderately large samples only [11,12]. The counterpart of extreme value theory requires in general much more data to achieve the same level of con dence.

It is worth mentioning some related work. A retrospective analysis of patients with bilateral testicular cancer is discussed in [13]. It has been found that germ cell testicular cancer patients have an increased risk of developing a contralateral testicular cancer. As noted earlier, familial connection is discussed in [5].

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Cite this article

Kedem B, De Oliveira V (2018) On Joint Analysis of Testicular Germ Cell Cancer. J Urol Res 5(1): 1097.