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Original Research

The utility of artificial neural networks and classification and regression trees for the prediction of endometrial cancer in postmenopausal women

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ABSTRACT

Objective: Artificial neural networks (ANNs) and classification and regression trees (CARTs) have been previously used for the prediction of cancer in several fields. In our study, we aim to investigate the diagnostic accuracy of three different methodologies (i.e. logistic regression, ANNs and CARTs) for the prediction of endometrial cancer in postmenopausal women with vaginal bleeding or endometrial thickness ≥5 mm, as determined by ultrasound examination.

Study design: We conducted a retrospective case-control study based on data from analysis of pathology reports of curettage specimens in postmenopausal women.

Methods: Classical regression analysis was performed in addition to ANN and CART analysis using the IBM SPSS and Matlab statistical packages.

Results: Overall, 178 women were enrolled. Among them, 106 women were diagnosed with carcinoma, whereas the remaining 72 women had normal histology in the final specimen. ANN analysis seems to perform better with a sensitivity of 86.8%, specificity of 83.3%, and overall accuracy (OA) of 85.4%. CART analysis did not perform well with a sensitivity of 78.3%, specificity of 76.4%, and OA of 77.5%. Regression analysis had a poorer predictive accuracy with a sensitivity of 76.4%, a specificity of 66.7%, and an OA of 72.5%.

Conclusion: Artificial intelligence is a powerful mathematical tool that may significantly promote public health. It may be used as a non-invasive screening tool to guide clinicians involved in primary care decision making when endometrial pathology is suspected.

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Introduction

Endometrial carcinoma is the most prevalent malignancy of the reproductive tract in women with an estimated prevalence of 25.7 new cases per 100,000 women per year according to the National Institutes of Health cancer statistics.[1] Although the disease is far from being characterized as an epidemic, its increasing rates internationally indicate it as an important emerging public health issue.[2] The actual drivers of the increasing incidence rates of endometrial carcinoma have not been clarified. However, one may assume that this can be partly attributed to population aging. Most cases are detected early in the course of the disease as postmenopausal bleeding is the most frequent symptom.[3] However, postmenopausal bleeding *per se* is not a useful marker for the detection of endometrial carcinoma because it is a relatively frequent clinical condition involving approximately 10% of women.[4] This means that 90% of women who are subjected to invasive procedures, and their accompanying morbidity, do not have cancer. In this context, several investigators have proposed different screening tools in primary care to determine which women will undergo further assessment.[5,6]

Various risk factors have been reported for endometrial carcinoma, including postmenopausal bleeding, diabetes mellitus, arterial hypertension, smoking, nulliparity, and late menopause.[7,8] Endometrial thickness has been suggested as a method to screen women; however, its diagnostic efficacy is very limited as false positive results have been reported to reach 70%.[9] After combining different parameters, however, the predictive value of these indices seems to be better as recent studies report an estimated sensitivity and specificity ranging between 70% and 80% in large cohorts.[7,10]

During the last decade, advanced classification techniques have been used for the prediction of various diseases. Implementation of models that incorporate artificial intelligence, including artificial neural networks (ANNs)[11–17] and classification and regression trees (CARTs), have been previously reported in medical specialties related to cancer.[1,8,18,19]

In our study, we aim to investigate the diagnostic accuracy of three different methodologies (i.e. logistic regression, ANNs, and CARTs) for the prediction of endometrial carcinoma in postmenopausal women with vaginal bleeding or endometrial thickness ≥5 mm as determined by ultrasound examination.

Methods

Study design

We conducted a retrospective case-control study in the section of gynecologic oncology of the third department of obstetrics and gynecology in our hospital. The study took place between January 2013 and December 2016 and was in agreement with both Greek and European Union Legislation as indicated in the Declaration of Helsinki for Human and Animal Rights and its later amendments. The study received an institutional review board approval its onset.

Patients

A consecutive series of postmenopausal women with vaginal bleeding or endometrial thickness ≥5 mm were included in the present study. Among them, several patients were diagnosed with endometrial carcinoma, whereas the remaining sample of women had no malignancy on the final pathology report. Women with endometrial hyperplasia, with or without atypia, were excluded from the present study, as well as women who received hormone therapy, or were treated for any type of cancer or autoimmune disease.

Data analysis

Statistical analysis

We assessed the normality of the distribution of continuous data using the Kolmogorov-Smirnoff test and graphical data. The Mann–Whitney U test was used for inferential statistics of continuous data, and the Chi-squared test was used for categorical variables (indication for dilatation and curettage [DC], diabetes, hypertension, hyperthyroidism, smoking, dyslipidemia, obesity, and late menopause, see Supplementary Table 1). The statistical analysis was performed in SAS, 9.4, for Windows (SAS Institute Inc. NC, USA).[20,21] All tests were double sided, and the level of statistical significance was set to 0.05.

We selected three different methods to examine and compare their predictive accuracy in diagnosing endometrial carcinoma.

Logistic regression

Regression analysis is widely adopted for the prediction of several diseases; hence, its implementation in the present article was deemed necessary for the prediction of endometrial carcinoma with CARTs and ANNs. In this study, the logistic regression analysis was performed with the Enter method in the SAS, 9.4, environment.

Classification and regression trees

We selected CARTs[22] because they are an explanatory technique, able to reveal data structure, identify important characteristics, and develop rules. CARTs can be used quickly and repeatedly. A classification tree is constructed from many repeated splits related to the target variable; these splits are producing rules of the form if X is less than value A or Y is within a range [C, D], then the sample is classified as normal with probability p. These splits end when no further split can be performed, either because all their observations belong to the same group or because the number of observations at the same node is small (according to a predefined value). These represent the terminal nodes of the tree.

CARTs have several advantages as predictive models for the diagnosis of a disease. First, the resulting algorithms are easy to understand as they represent a sequential method that ultimately results in the determination of the optimal algorithm. Second, in every step of the resulting algorithm, the associated risk (probability) of a case belonging to the targeted groups is known; therefore, it is up to the clinician to decide if the results are satisfactory. And, finally, their hierarchical approach is easily redefined by clinicians in future