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***Biostatistician's Eyes** / Biyoistatistikçi Gözünden*

Factors associated with advanced tricuspid regurgitation after left-side double valve replacement in propensity-score-matched analysis: Propensity score matching in observational studies

Eğilim skoru eşleştirme analizinde sol taraflı çift kapak replasmanı sonrasında ileri triküspid yetmezliği ile ilişkili faktörler: Gözlemsel çalışmalarda eğilim skoru eşleştirmesi

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In recent years, research has focused on the causality relationship between variables. It is possible to divide the variables in a causal relationship into two as "independent" variable(s) which is in the "cause" state and "dependent" variable(s) which is in the "result" state. The investigation of the effect of the change in the independent variable(s) on the dependent variable forms the basis of the causality structure. Researches on causality can be examined under two main headings as experimental and observational studies. Experimental studies, known as studies investigating the effectiveness of diagnosis and treatment methods, are studies conducted under conditions determined by the experimenter and in which the intervention to subjects/individuals is possible. For instance, in an experimental study in which the effect of the drug is investigated, the drug is given to the individuals and what type of changes it causes in the outcome variable (such as increased blood sugar due to the drug effect) are evaluated. Experimental studies, in which it is possible to partially control the factors affecting the outcome variable, can also be divided into studies with a control group and studies without a control group. It is not possible to make comparisons between methods in experimental studies that do not include a control group. On the other hand, in experimental studies involving a control group, it is determined whether the effect of the applied method or treatment method on the outcome variable is caused by the method or other factors. Studies involving a control group are preferred to studies without a control group, as such studies can provide better control over the independent variable(s), are used more frequently, particularly in regression analysis, and contain more information about cause-effect relationships than observational studies. However, observational studies are preferred instead of experimental studies in some special cases that may arise, such as the failure to provide the desired laboratory conditions for the experiment, the possibility of harming the health of the subject. In observational studies, data are obtained from records or patient files. In such studies, observation is made without interfering with the natural course of the event. In other words, no additional monitoring, testing or treatment is used, while the data are being observed. Since the factors examined in observational studies cannot be controlled, they cannot be changed at any time. In addition, it is not possible to repeat the observations under the same conditions. It is possible to classify observational studies that examine the incidence, distribution or causes of diseases in the population as descriptive, case-control, cross-sectional and cohort studies. In addition, it is not under the control of the researcher as to which group the observed units would be assigned to. As a result, there may be large differences in the observed cofounder of

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the units in the experimental and control groups. This difference, which may affect the results of the study before the treatment, would cause systematic errors. The source of systematic errors should be investigated and eliminated. Since a limited number of covariates are used in methods such as stratification, regression correction and matching, which are used to correct the systematic error, their usage areas are limited. Propensity score analysis is an effective method used to reduce the bias of treatment effects in observation-based datasets, since it does not limit the number of covariates. Propensity score analysis, a scheme used to generate paired datasets and strata containing a large number of covariates, includes a summary measure of information on covariates.[1]

The propensity score is the probability of treatment assignment conditional on observed baseline characteristics. Adjustments to eliminate bias can be made by using the propensity score instead of using all the covariates one by one.[2] To reduce the bias in the estimation of treatment effects, with the help of the propensity score method proposed by Rosenbaum and Rubin, the error is reduced by balancing the units in the two groups in terms of the variables used. On the other hand, it is possible to test whether there is a difference between two groups (the treatment and control) by using the Mann-Whitney U test, t-test, chi-square test or other pairwise comparison tests.

Propensity score, in a n-unit data set with no missing observations, i. the individual's propensity score value is the conditional probability of being assigned a particular treatment (Yi=1) versus the control group (Yi=0) according to the observed covariate vector xi. In other words, propensity scores are defined as the conditional probability of assigning a unit to a particular treatment condition, given the observed variables. The propensity score can be used in both observational studies and experimental studies. Propensity score can be obtained using the logistic regression model, probit model, discriminant analysis, and cluster analysis.[3] The purpose of calculating the propensity score is to be able to conclude that two units, one in the treatment group and the other in the control group, with the same or very close propensity scores, are randomly assigned to each group. If there is no data loss in the independent variables and the distribution of the independent variables fits the multivariate normal distribution, discriminant analysis is used while estimating the propensity score. In addition, the covariances of the independent variables should be equal at each group level. If nominal or ordinal scaled variable(s) are used among the independent variables in the discriminant analysis, these two assumptions cannot be met. In this case, logistic regression analysis is used instead of discriminant analysis. In the logistic regression analysis, it is not necessary to provide these assumptions for the independent variables. Logistic regression analysis provides an alternative to discriminant analysis and crosstabs in case of various assumptions distortions (such as normal distribution and lack of common covariance). In case the dependent variable is binary or discrete variable containing more than two levels, it is an alternative to linear regression analysis, since the assumption of normality is not provided. On the other hand, when the number of groups (clusters) to which the observed units would be assigned is not known exactly, cluster analysis can be used in propensity score estimation. In discriminant and logistic regression analysis, the number of groups to be assigned is known. In practice, the propensity score is most often estimated using a logistic regression model, in which treatment status is regressed on observed baseline characteristics. The estimated propensity score is the predicted probability of treatment derived from the fitted regression model.[4] As the number of covariates in the model increases, it may become difficult to find units with similar characteristics for units in the treatment group. Adjustments to eliminate bias in the sample with the propensity score can be made by using the propensity score instead of using all the covariates one by one. Four different propensity score methods are used for removing the effects of confounding while estimating the effects of treatment on outcomes: propensity score matching, stratification (or subclassification) on the propensity score, inverse probability of treatment weighting using the propensity score, and covariate adjustment using the propensity score.[5] With the propensity score calculated by choosing one of these methods, resampling is performed and the effect of the factor is estimated for the new sample obtained. If there are two units with the same propensity score, one in the case group and one in the control group, then it is thought that the two units are randomly assigned to each group, that is, they are in the case or control groups with equal similarity. Therefore, propensity score can be said to be a balancing score.[6]

In the article entitled “Factors Associated with Advanced Tricuspid Regurgitation After Left-Side Double Valve Replacement in Propensity-Score-matched Analysis,” the authors aimed to investigate the association of progression of tricuspid regurgitation (TR) following double valve replacement by comparing the tricuspid valve (TV) repair and no-TV repair groups. They also aimed to analyze the outcomes of repair groups and patients with unrepaired mild-to-moderate TR. A total of 157 patients, 52% of whom were women, participated in the study and the data were evaluated using propensity score analysis. A comparison of baseline clinical and echocardiographic parameters between TV repair and no-TV repair groups was made, and it was observed that AF was significantly lower in the no-TV repair group, while the TV repair group had a significantly longer cardiopulmonary bypass duration. In addition, there was no statistically significant difference between the groups in valvular etiology. On the other hand, the no-TV repair group had significantly decreased pulmonary artery pressure and decreased TR degree. The no-TV repair group had a significantly smaller tricuspid annulus diameter, and a smaller left atrial diameter. It was also observed that neurological complications did not make a significant difference between the groups. However, the TV repair group had a lesser degree of TR and the mechanical ventilation and intensive care unit (ICU) stay were significantly shorter in the no-TV repair group. While group comparisons of continuous variables were made using the Mann-Whitney U test, categorical variables were compared using the chi-square test.

In the next step of the study, two groups were evaluated with the help of propensity score analysis. Baseline characteristics, postoperative ICU and hospital stay, ventilation time, and mortality were examined through propensity score analysis. As previously mentioned, when assumptions such as the measurement type of the independent variable or the normal distribution of the dependent variable are not provided, logistic regression analysis is used to estimate the propensity score. The relationship between eight predictors (age, sex, atrial fibrillation, ejection fraction, diameter of tricuspid annulus, rheumatic etiology, left ventricular end-diastolic diameter, left ventricular end-systolic diameter) and moderate and severe TR was examined in the logistic model. Rheumatic etiology was statistically significant for TR progression in the univariate analysis and it was an independent factor for postoperative progression of TR on multivariable analysis. No-TV repair (reference repair) and rheumatic etiology were independently associated with presence of progression TR in all groups for propensity score matched data in the conditional multivariable logistic regression analysis. In this study, with the help of propensity score analysis, rheumatic etiology was shown to be an independent marker for the progression of TR. On the other hand, it was also independently associated with progression of TR in patients with mild-to-moderate no-TV repair TR. According to the results of TV repair and no TV repair binary group comparisons, the postoperative TR grade decreases with TV repair and the two groups were found to have a similar operative mortality rate and potential complications.

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