

## Analysis With the Propensity Score of the Association Between Likelihood of Treatment and Event of Interest in Observational Studies. An Example With Myocardial Reperfusion

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**Introduction and objectives.** Analysis of the effect of treatment in observational studies is complex due to differences between treated and nontreated patients. Calculating the probability of receiving treatment conditioned on relevant covariates (propensity score [PS]) has been proposed as a method to control for these differences. We report an application of PS to assess the association between reperfusion treatment and 28-day case fatality in patients with acute myocardial infarction (AMI).

**Method.** We describe the procedure used to calculate PS for receiving reperfusion treatment, and different strategies

to analyze the association between PS and case fatality with regression modeling and matching. Data were from a population-based registry of 6307 patients with AMI in Spain during 1997-98.

**Results.** The PS for reperfusion was calculated in 5622 patients. In the multivariate analysis, reperfusion was associated with lower case fatality (OR=0.59; 95% confidence interval [95% CI], 0.46-0.77). When PS was included as a covariate, this association became non-significant (OR=0.76; 95% CI, 0.57-1.01). In the subgroup of matched patients with a similar PS (n=3138), treatment was not associated with case fatality (OR=0.95; 95% CI, 0.72-1.26). When the influence of cases with missing data on PS was controlled for, reperfusion treatment was associated with lower fatality (OR=0.66; 95% CI, 0.55-0.80).

**Conclusions.** Calculating propensity score is a method that controls for differences between treated and nontreated patients. This score has limitations when matching is incomplete and when data are missing. Results of the present example suggest that reperfusion treatment reduces AMI case fatality.

**Key words:** Myocardial infarction. Prognosis. Reperfusion. Thrombolysis.

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## ABBREVIATIONS

AMI: acute myocardial infarction.  
 CCU: coronary care unit.  
 IBERICA: Research, Specific Search and Registry of Acute Coronary Events.  
 OR: odds ratio.  
 PCI: percutaneous coronary intervention.  
 PS: propensity score.  
 ROC: receiver operating characteristic.

### Análisis de la asociación entre un tratamiento y un acontecimiento de interés en estudios observacionales utilizando la probabilidad de recibir el tratamiento (*Propensity Score*). Un ejemplo con la perfusión miocárdica

**Introducción y objetivos.** Determinar el efecto de un tratamiento en estudios observacionales es problemático por las diferencias existentes entre tratados y no tratados. Un método propuesto para controlar estas diferencias es calcular la probabilidad condicionada por covariables de recibir el tratamiento, *Propensity Score* (PS). Presentamos una aplicación de este método analizando la asociación entre perfusión y letalidad a 28 días en pacientes con infarto agudo de miocardio (IAM).

**Método.** Se presenta cómo calcular la PS de recibir perfusión y las diferentes estrategias para analizar posteriormente su asociación con la letalidad mediante modelos de regresión y apareamiento. Utilizamos datos de un registro poblacional de IAM realizado en España entre 1997 y 1998 que incluyó 6.307 IAM.

**Resultados.** Se calculó la PS de perfusión en 5.622 pacientes. En el análisis multivariado la perfusión se asoció con menor letalidad (*odds ratio* [OR] = 0,59; intervalo de confianza [IC] del 95%, 0,46-0,77); al ajustar además por la PS de perfusión esta asociación no fue significativa (OR = 0,76; IC del 95%, 0,57-1,01). En el subgrupo de pacientes apareados, tratados y no tratados con PS de perfusión similar (n = 3.138), este tratamiento no se asoció con letalidad (OR = 0,95; IC del 95%, 0,72-1,26). Controlando el impacto de los casos con datos insuficientes en la PS de perfusión, ésta se asoció con menor letalidad (OR = 0,66; IC del 95%, 0,55-0,80).

**Conclusiones.** El cálculo de la PS es un método para controlar las diferencias entre los grupos tratado y no tratado. Tiene limitaciones cuando el apareamiento es incompleto o hay datos insuficientes en la PS calculada. Los resultados del ejemplo presentado indican que la perfusión reduce la letalidad del IAM.

**Palabras clave:** *Infarto de miocardio. Pronóstico. Reperfusión. Trombólisis.*

## INTRODUCTION

The evidence on the efficacy of a treatment or intervention derives from randomized clinical trials, which have the best design to assess treatment efficacy.<sup>1</sup> One of the limitations of this approach is the generalization of the results to the rest of the population (external validity).<sup>1</sup> For this reason, the evaluation of the effect of treatment in the general population—its effectiveness—by means of observational studies is also of interest.<sup>2</sup> Observational studies have classically been reported to overestimate the treatment effect,<sup>3</sup> although some authors have found no differences between the results of observational studies and randomized clinical trials.<sup>4</sup> The major limitation of observational studies is the fact that treatment is not randomly assigned. Thus, there is a selection bias that may indicate that the observed treatment effect could be related to the baseline characteristics of the treated and untreated patients rather than to the treatment itself. Multivariate statistical analysis is normally employed to control the differences, but these methods are not perfect.

In 1983, Rosenbaum and Rubin<sup>5</sup> proposed a new method for controlling this bias: calculating the individual probability, influenced by certain covariates, of receiving a treatment, the propensity score (PS). In recent years, the use of this method in observational studies is increasing considerably.<sup>6</sup>

The main objective of this report is to present a practical application of this statistical method, discussing its advantages and limitations. We analyze the association between myocardial reperfusion therapy and 28-day lethality in patients with acute myocardial infarction (AMI) ranging between 25 and 74 years of age who reached a hospital alive within the first 12 hours of onset of symptoms and were enrolled in the IBERICA (Research, Specific Search and Registry of Acute Coronary Events) study.

## METHOD

### Study Design

The study design, methods and quality controls have been described in detail elsewhere.<sup>7-9</sup> Briefly, the IBERICA study, which was initiated in 1996, is a population-based registry that records cases of AMI in individuals between the ages of 25 and 74 years residing in 7 regions of Spain: Castile-La Mancha (Toledo and Albacete), Girona, Majorca, Murcia, Navarre, the Basque Country, and Valencia (metropolitan area).<sup>8,9</sup>

We present the data from patients who reached the hospitals of the participating localities alive. The study period began on 1 January 1997 and ended on 31 December 1998.

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