Med Intensiva. 2018;42(2):134–136

medicina intensiva

www.elsevier.es/medintensiva

LETTERS TO THE EDITOR

Comparative statistical analysis in observational epidemiological studies☆

Análisis estadísticos comparativos en los estudios epidemiológicos observacionales

Dear Editor,

We wish to congratulate Socias et al.[1] for their work on the prognostic impact of ST segment elevation acute coronary syndrome (STE-ACS) in Mallorca, Spain.

Subpopulations with STE-ACS from two observational registries were compared in different time frames. In the *IBERICA-Mallorca* registry, fibrinolysis was the main reperfusion therapy, while the *Código infarto-Illes Balears (CI-IB)* registry implemented one healthcare network for the management of STE-ACS based on primary angioplasty (PA). From both registries, only 49.7 and 58.8 per cent of the populations were included for the analysis. Features from both samples varied significantly in aspects such as history; clinical profile; and effective medical therapy in the management of STE-ACS (betablockers and ACE).[2]

The main conclusion from the study[1] is that the implementation of one PA network reduced mortality rate. However, the statistical analysis conducted deserves certain considerations:

(a) *Survival analysis*: in observational studies where the main goal is to assess the time elapsed until the occurrence of one event, *survival analyses*[3,4] are normally used. The most widely used statistical tool to know the effect of one independent variable in time is the *Kaplan–Meier method*. However, it is not good for the simultaneous assessment of more than one independent variable, or to estimate the effect size on the risk of occurrence of one event.[3] In a setting where different variables coexist that may have an impact on the main goal, the survival analysis using the *Cox regression* model is key to assess to what extent multiple variables can modify the risk of occurrence of a single event.[4] This study showed that the mortality rate at 28 days varied after the implementation of this network (*IBERICA-Mallorca* = 12.2 vs *CI-IB* = 7.2 per cent; HR = 0.560; 95 per cent CI: 0.360–0.872; $p = 0.010$) based on the *Kaplan–Meier method*. However, when the *Cox regression analysis* was conducted, no statistical significance was achieved in either model.

(b) *Propensity score matching*: one option for the inter-group comparison of one outcome variable is observational studies is the *Propensity score matching*.[5] This statistical analysis assesses the effect that one treatment strategy has based on the covariables that predict that one patient will be assigned to the assessed treatment, and not the control group. Thus, by pairing patients based on the estimated propensity scores, we can make inter-group comparisons with an approximate balance on the relevant variables, instead of just one simple comparison between patients who received the treatment strategy, and those who did not.

In sum, even though the implementation of one PA network for the management of STE-ACS improved prognosis,[2] the *Kaplan–Meier* analysis was not powerful enough to confirm that the reported reduced mortality rate is exclusively due to the effect of such healthcare network. This is why we believe that conducting one *Cox regression analysis* to assess not only the baseline differences and type of reperfusion, but also different therapies received; or one *propensity score matching* analysis to balance all relevant covariables will make better evaluations of the real impact of this network on the prognosis of this population.

Conflicts of interest

The authors declare no conflict of interests associated with this article whatsoever.

References

1. Socias L, Frontera G, Rubert C, Carrillo A, Peral V, Rodriguez A, et al. Comparative analysis between 2 periods of acute myocardial infarction after a decade in Mallorca. IBERIA Study (1996–1998) and Infarction-Code (2008–2010). Med Intensiva. 2016;40:541–9.
2. Steg PG, James SK, Atar D, Badano LP, Blömstrom-Lundqvist C, Borger MA, et al. ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. Eur Heart J. 2012;33:2569–619.

☆ Please cite this article as: Bosch-Gaya A, Matute-Blanco L, Fernández-Rodríguez D, Worner F. Análisis estadísticos comparativos en los estudios epidemiológicos observacionales. Med Intensiva. 2018;42:134–135.

3. Kaplan EL, Meier P. Non-parametric estimation from incomplete observations. J Am Stat Assoc. 1958;53:457–81.
4. Cox DR. Regression models and life-tables. J R Stat Soc. 1972;34:187–220.
5. Austin PC. An introduction to propensity score methods for reducing the effects of confounding in observational studies. Multivariate Behav Res. 2011;46:399–424.

A. Bosch-Gaya, L. Matute-Blanco,
D. Fernández-Rodríguez*, F. Worner

Servicio de Cardiología, Hospital Universitari Arnau de Vilanova, Lérida, Spain

*Corresponding author.
E-mail address: d.fernan.2@hotmail.com
(D. Fernández-Rodríguez).
2173-5727/

Improvement of the safety of a clinical process using failure mode and effects analysis: Prevention of venous thromboembolic disease in critically ill patients☆

Mejora en la seguridad de un proceso clínico utilizando el análisis modal de fallos y efectos: profilaxis de la enfermedad tromboembólica venosa en pacientes críticos

Dear Editor,

In the first place, we would like to thank you for your interest in our work. The goal of this work was to use the methodology from the Modal Analysis of Errors and Effects and implement a series of measures in order to improve this process and optimize the patient's safety (PS) on everything that has to do with the venous thromboembolic disease (VTED). One of these measures was the implementation of a 2014 protocol that was not fully developed in our paper because it was not the main goal of our work. However, while we were developing such protocol, seven special situations were established, among them, the management of renal failure (RF) that suggested the adjustment of enoxaparin based on the creatinine clearance (CrCl) rate, and according to the recommendations established by the Spanish Agency of Medicine and Medical Devices, and the Spanish Society of Hospital Pharmacy.[1] At the same time, if the patient remained under continuous renal replacement therapy, the same dose than without RF was used since no bioaccumulation has been confirmed so far.[2] Even so, we rather measure the concentrations of the anti-factor Xa as a safety measure because even though it has some limitations such as the absence of a clear correlation between the levels of anti-Xa and adverse events, or the poorly-established range of prophylactic levels, until these issues are resolved, it is still the best tool we have today to assess the effect of low-molecular-weight heparin (LMWH).

Enoxaparin was the only LMWH used in our study, which is the usual practice in 90 per cent of the intensive care units (ICU) in Madrid and nationwide, where enoxaparin and bemiparin are used in 95.2 per cent of ICUs.[3] Such a decision may be triggered by a lack of evidence favoring one particular molecule over another in terms of effectiveness. All the indications for enoxaparin have already been approved as its technical label confirms and, in these cases, we can reduce its dose as long as we follow the guidelines for VTED prevention and those from the very paper they mention. Also, while enoxaparin; dalteparin; tinzaparin; or nadroparin are comparable, they are not interchangeable, require different doses and use different units of measurement. This may be problematic when it comes to PS, which is precisely what the Medication Errors Reporting Program claimed after confirming deaths of patients, due to confusion when using different heparin molecules.[4] Finally, there is still controversy on issues such as bioaccumulation, and recent studies have concluded that the prophylactic use of enoxaparin in patients with CrCl rates $\leq$30 ml/min[5] is safe.

One of the characteristics of the ICU patient is his dynamicity. Just as we said in our work, another one of the measures for improvement suggested was the introduction of one daily PS checklist, and another bedside PS check-list, which is when we will proceed to adjust the VTED prevention measures.

For all the aforementioned, and with the only goal of optimizing the safety of our patients, we believe that the strategy adopted is the right one based not only on the evidence available, but also on our own experience after the implementation of the protocol.

Funding

Grants for the development of research projects awarded by The Healthcare Research Institute of Hospital 12 de Octubre, i+12, sponsored by AMGEN S.A.

References

1. Manresa Ramón N, Nájera Pérez MD, Page del Pozo MA, Sánchez Martínez I, Sánchez Catalicio MM, Roldán Schilling V. Establecimiento de un protocolo para el uso de la heparina en pacientes con características especiales. Farm Hosp. 2014;38:135–44.
2. Isla A, Gascón AR, Maynar J, Arzuaga A, Corral E, Martín A, et al. In vitro and in vivo evaluation of enoxaparin removal by continuous renal replacement therapies with acry-

☆ Please cite this article as: Viejo Moreno R, Sánchez-Izquierdo Riera JA, Molano Álvarez E, Barea Mendoza JA, Temprano Vázquez S, Díaz Castellano L, et al. Mejora en la seguridad de un proceso clínico utilizando el análisis modal de fallos y efectos: profilaxis de la enfermedad tromboembólica venosa en pacientes críticos. Med Intensiva. 2018;42:135–136.