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EDITORIAL

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Logistic or Cox model to identify risk factors of nosocomial infection: still a controversial issue

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During the past decades, relative risk regression models have become indispensable tools for the analysis of clinical studies to identify risk factors of any adverse event. However, there are still two competing standard philosophies of regression modelling in clinical research: the logistic model and the Cox model. Whether or not one of these two models is more appropriate in identifying risk factors of nosocomial infection (NI) in intensive care units (ICUs) is still a matter of debate. This is exemplified in this issue of *Intensive Care Medicine* with the article by Irala-Estevez and colleagues [1], who present some comparisons of these models.

Actually, logistic and Cox regressions are mathematical modelling approaches that both relate a set of risk factors to some specified event through a log-linear function. However, there are two fundamental differences between these two models. First, they measure association with the use of a different metric: while Cox models measure the relative risk of NI in (infinitesimally) small time intervals under the assumption that it is constant over the follow-up period, logistic regression models measure the relative odds of NI after a fixed duration of follow-up. Therefore, when event rates are high, the relative odds can differ substantially from the relative risk, explaining discrepancies in selected risk factors. Second, the Cox model allows for different lengths of follow-up, i.e., for (right) "censored" data (indicating that some times to event are not known but are only known to be greater than the observation period), under the assumption of non-informative censoring (i.e., that the mechanism of censoring is independent of the event process); by contrast, the logistic model assumes constant follow-up for all individuals, treating the event as binary or dichotomous (i.e., take two possible values, event or no event). Despite these differences, parameter estimates from the two models can be similar when the outcome event is rare, the effect of the risk factors is weak and the follow-up period is short [2, 3, 4].

Actually, in identifying risk factors of NI in ICU, the "logistic-pros" are much the larger group, and most of the statistical analyses which appear in the medical literature are based on this model [5, 6, 7, 8, 9, 10]. The pros of the Cox model are fewer in this setting [11, 12, 13] in contrast to other medical fields like oncology or haematology.

How to explain this traditional concern about the use of the logistic model or the Cox model for identifying risk factors in ICU?

There should be two main reasons. The first reason is that many authors have used a case-control design, even recently [14], so that the logistic model long appeared as the only standard approach to handle the resulting correlated data. Of note, new statistical approaches have been developed to extend the use of the Cox model to such data, and these recently have overcome this issue [15].

The second, and probably the most interesting reason, that could be advocated alternately for using or not using the Cox model when identifying risk factors

of NI from cohort data in ICU, relies on the specific mechanisms of censorship in the ICU. Indeed, ICU patients are usually followed-up until they die or they are discharged from ICU or from hospital, resulting in commonly large differences in the observation periods among patients. While the "Cox-pros" consider that these differences avoid the use of the logistic model (that assumes them constant), the "logistic-pros" argue for the violation of the underlying assumption of the Cox model (i.e., censoring is independent or non-informative of the infection process). For instance, they argue that patients free of NI at discharge from ICU would not develop NI on the following days similarly to those who were kept in ICU. The early censoring of those patients provided by the Cox model would result in biased estimates of risk factors. One way – which is close to the philosophy of logistic modelling – of overcoming this issue is to follow-up all ICU patients until a calendar point (such as day 30) which marks the end of the study; then, the mechanism of censoring could become independent of the infection process. Nevertheless, this does not account for deaths that preclude the occurrence of NI. If such deaths fundamentally alter the probability of NI occurrence, i.e., in the setting of so-called "competing risks", the use of the standard Cox model has been shown inappropriate [16, 17] and new approaches of regression should be used [18].

In summary, the main reason for the controversy in using standard logistic and Cox approaches when analysing risk factors of NI in ICU patients could be summarised in the distinct assumptions regarding the non-infected patients. While "logistic-pros" suppose that non-infected patients could be melt altogether (whatever their lengths of exposure and regardless of whether they were discharged alive or dead from ICU), the "Cox-pros" prefer to assume that the reasons of follow-up discontinuation do not rely on the infection process, whatever the reason. Both simplify a complex reality, that should be more specifically addressed in the next future by a more adapted methodology.

References

1. Irala-Estevez J, Martinez-Concha D, Diaz-Molina C, Masa-Calles J, Serrano del Castillo A, Navajas RFC (2001) Comparison of different methodological approaches to identify risk factors of nosocomial infection in intensive care units. Intensive Care Med 27: 1254–1262, DOI 10.1007/s001340101007
2. Green MS, Symons MJ (1983) A comparison of the logistic risk function and the proportional hazards model in prospective epidemiologic studies. J Chronic Dis 36: 715–723
3. Hauck WW (1985) A comparison of the logistic risk function and the proportional hazards model in prospective epidemiologic studies. J Chronic Dis 38: 125–126
4. Ingram DD, Kleinman JC (1989) Empirical comparisons of proportional hazards and logistic regression models. Stat Med 8: 525–538
5. Tejada Artigas A, Bello Dronda S, Chacon Valles E, Munoz Marco J, Villuendas Uson MC, Figueras P, Suarez FJ, Hernandez A (2001) Risk factors for nosocomial pneumonia in critically ill trauma patients. Crit Care Med 29: 304–309
6. Fagon JY, Chastre J, Wolff M, Gervais C, Parer-Aubas S, Stephan F, Similowski T, Mercat A, Diehl JL, Sollet JP, Tenaillon A (2000) Invasive and noninvasive strategies for management of suspected ventilator-associated pneumonia. A randomized trial. Ann Intern Med 132: 621–630
7. Akca O, Koltka K, Uzel S, Cakar N, Pembeci K, Sayan MA, Tutuncu AS, Karakas SE, Calangu S, Ozkan T, Esen F, Telci L, Sessler DI, Akpir K (2000) Risk factors for early-onset, ventilator-associated pneumonia in critical care patients: selected multiresistant versus nonresistant bacteria. Anesthesiology 93: 638–645
8. Markowicz P, Wolff M, Djedaini K, Cohen Y, Chastre J, Delclaux C, Merrer J, Herman B, Veber B, Fontaine A, Dreyfuss D (2000) Multicenter prospective study of ventilator-associated pneumonia during acute respiratory distress syndrome. Incidence, prognosis and risk factors. ARDS Study Group. Am J Respir Crit Care Med 161: 1942–1948
9. Garrouste-Orgeas M, Chevret S, Mainardi JL, Timsit JF, Misset B, Carlet J(2000) A one-year prospective study of nosocomial bacteraemia in ICU and non-ICU patients and its impact on patient outcome. J Hosp Infect 44: 206–213
10. Legras A, Malvy D, Quinioux AI, Villers D, Bouachour G, Robert R, Thomas R (1998) Nosocomial infections: prospective survey of incidence in five French intensive care units. Intensive Care Med 24: 1040–1046
11. Bonten MJ, Bergmans DC, Ambergen AW, De Leeuw PW, Van der Geest S, Stobberingh EE, Gaillard CA (1996) Risk factors for pneumonia, and colonization of respiratory tract and stomach in mechanically ventilated ICU patients. Am J Respir Crit Care Med 154: 1339–1346
12. Combes P, Fauvage B, Oleyer C (2000) Nosocomial pneumonia in mechanically ventilated patients, a prospective randomised evaluation of the Stericath closed suctioning system. Intensive Care Med 26: 878–882
13. Nourdine K, Combes P, Carton MJ, Beuret P, Cannamela A, Ducreux JC (1999) Does noninvasive ventilation reduce the ICU nosocomial infection risk? A prospective clinical survey. Intensive Care Med 25: 567–573
14. Girou E, Schortgen F, Delclaux C, Brun-Buisson C, Blot F, Lefort Y, Lemaire F, Brochard L (2000) Association of noninvasive ventilation with nosocomial infections and survival in critically ill patients. JAMA 284: 2361–2367
15. Soufir L, Timsit JF, Mahe C, Carlet J, Regnier B, Chevret S (1999) Attributable morbidity and mortality of catheter-related septicemia in critically ill patients: a matched, risk-adjusted, cohort study. Infect Control Hosp Epidemiol 20: 396–401
16. Pepe MS, Mori M (1993) Kaplan-Meier, marginal or conditional probability curves in summarizing competing risks failure time data? Stat Med 12: 737–751
17. Gooley TA, Leisenring W, Crowley J, Storer BE (1999) Estimation of failure probabilities in the presence of competing risks: new representations of old estimators. Stat Med 18: 695–706
18. Moeschberger ML, Klein JP (1995) Statistical methods for dependent competing risks.Lifetime Data Anal 1: 195–204