Methodological Aspects in the use of Multiple Logistic Regression Analysis

Davi Jorge Fontoura Solla[1,2], Nivaldo Menezes Filgueiras-Filho[1], Anibal Silvany-Neto[2]

Serviço de Atendimento Móvel de Urgência (SAMU)[1]; Faculdade de Medicina, Universidade Federal da Bahia[2], Salvador, BA – Brazil

Dear Editor,

We would like to present a few considerations pursuant to the statistical analysis of the predictors of death in the article by Caluza et al[1], even though observing its nature of initial/pilot project.

It has not remained clear which variables were included in the initial model and which method was used to select those significant variables in the final adjusted model (*backward, forward, full model* or variants).

By virtue of the fine progression of the patients (in-hospital mortality of 6.8%) and of the relatively small sample size (n = 205), the number of deaths was low (n = 14). That is an excellent clinical result, but it imposes caution upon the logistic regression. The final model has presented six significant variables (perhaps the initial model might have had even more co-variables), with a maximum Events Per Variable (EPV) ratio of 2.3 (14/6). A low ratio of EPV results in an unstable model, with an increase in bias, variability, and overrating of the coefficients of regression and unverisimil Confidence Intervals (CI)[2,3]. The worst case scenario[4] would exactly be with 2 to 4 EPV, ≤ 30 outcomes, and low prevalence/incidence (< 10%) of the predictors (previous Cerebral Vascular Accident – CVA – [7.8%], Total Atrioventricular Block – total AV block – [6.8%], intra-aortic balloon pump – IABP – [5.8%], and cardiogenic shock [7.3%]).

The occluded artery related to the infarction and the zero tissue flow grade (*blush*) upon the initial injection in the artery related to the infarction were variables inserted in a parallel fashion in the model. Has multi-co-linearity been verified among these? Except in the filling by collaterals, the entire occluded artery will have zero tissue flow grade, resulting in a high redundancy, with a reduction in the reliability of the coefficients of regression and amplification of the standard errors[5].

The use of the IABP performs much more as a risk marker than actually as a risk factor, not being in the causal pathway of the outcome analyzed. Its inclusion in the analysis of the predictors of death is questionable, given the potential to influence the other co-variables.

Still pertinent to the IABP, considering the presence of the cardiogenic shock variable in the multivariate model, it would be interesting to verify whether considerable redundancy has not taken place as well, hence that complication is one of the main indications for the IABP.

Finally, the residual diagnostics of the logistic regression has either not been made or reported, as well as the CI of the *Odds Ratio* (OR) - fundamental items to assess the adjustment of the model, and which would facilitate the elucidation of the questions above.

As has been mentioned in another Letter to the Editor, any criticism to the statistical analysis of that work does not cloud the relevance of implementing a regionalized network of care to the Acute Myocardial Infarction with ST Segment Elevation (Acute STEMI). This is about an organization model of the care, which deserves to be replicated by Brazil.

References

1. Caluza AC, Barbosa AH, Gonçalves I, Oliveira CA, Matos LN, Zeefried C, et al. Rede de infarto com supradesnivelamento de ST: sistematização em 205 casos diminui eventos clínicos na rede pública. Arq Bras Cardiol. 2012;99(5):1040-8.

2. Peduzzi P, Concato J, Kemper E, Holford TR, Feinstein AR. A simulation study of the number of events per variable in logistic regression analysis. J Clin Epidemiol. 1996;49(12):1373-9.

3. Harrel FE Jr, Lee KL, Mark DB. Multivariable prognostic models: issues in developing models, evaluating assumptions and adequacy, and measuring and reducing errors. Stat Med. 1996;15(4):361-87.

4. Vittinghoff E, McCulloch CE. Relaxing the rule of ten events per variable in logistic and Cox regression. Am J Epidemiol. 2007;165(6):710-8.

5. Kleinbaum DG, Kupper LL, Nizam A, Muller KE. Applied regression analysis and other multivariable methods. 4th ed. Belmont: Thomson Brooks/cole; 2008.

Reply

We appreciate the questions asked[1] on the statistical analysis of the article[2], which were adequately formulated, and we agree that the systematization in networks of the treatment of the Acute Myocardial Infarction (AMI) with elevation is unarguably a solution to favor the immediate improvement in the Brazilian results as a whole.

The concerns presented and those we have had are the same because, as also inferred from the very article, a sample of 205 cases does not provide unarguably reliable data. That is exactly why we have not provided detail or mentioned specific points of the multivariate analysis and of the logistic regression. We have used the SPSS-20 software, two-tailed, *backward*, whilst knowing that a small sample, points outside the curve, an inappropriate model, and multiple points for analysis may eventually distort results in that situation. The number of Events Per Variable (EPV) may also affect the results obtained; we have attained Confidence Intervals (CI) which were too variable, such as, for example, ejection fraction with an *Odds Ratio* (OR) of 0.90 and a CI from 0.35 to 0.94, and *blush* with an OR of 9.45 and a CI from 1.21 to 59,45. We also agree - as has been mentioned - that, when we speak of advanced Killip and cardiogenic shock (intra-aortic balloon pump as a marker) or low TIMI flow and myocardial blush, there is an overlap of co-linearity and interaction, whilst it is up to the conductor of the study to choose which item applies better to the situation, in order to obtain the one which has the lowest variability and, therefore, the greatest reliability, with some interaction in that order of variables always being there. However, we respectfully and completely disagree with the argument of there having been a low prevalence of events: as a record with unscreened patients, we have had, in this population, 31.7% of diabetic subjects, 7.8% of previous Cerebral Vascular Accident (CVA), 11.2% of pre-existing renal dysfunction; in this population, 6.8% of Total Atrioventricular Block (total AV block) and 7.3% of cardiogenic shock have occurred - a proportion of problems and complications which is greater than those in many of the studies of AMI with elevation, as mentioned in texts of guidelines[3-6], befitting with the sample of a record. It has rather occurred that the sample was small, and so was the proportion of deaths.

An important, supplementary fact - and which makes us confident in relation to that which has been published - is that, today, with 620 cases (three times the size of the sample of the *Arquivos*) in the record, the data of mortality and of the statistical analysis of the article remain, in general, very close to that which has been published. A new article, involving the risks related to mortality and with analysis in further detail, which follows the suggestions of the questions above, is already finished and on the verge of being sent for publishing.

Truly,

Ana Christina Vellozo Caluza
Antonio Carlos Carvalho
Pelos demais autores do artigo

References

1. Solla DJ, Figueiras NM, Silvany-Neto A. Aspectos metodológicos na utilização da análise de regressão logista múltipla. Análise de regressão logística múltipla. Arq Bras Cardiol. 2013;xx(xx):xx.

2. Caluza AC, Barbosa AH, Gonçalves I, Oliveira CA, Matos LN, Zeefried C, et al. Rede de infarto com supradesnivelamento de ST: sistematização em 205 casos diminui eventos clínicos na rede pública. Arq Bras Cardiol. 2012;99(5):1040-8.

3. Steg G, James SK, Atar D, Badano LP, Blömstrom-Lundqvist C, Borger MA, et al; Task Force on the management of ST segment elevation acute myocardial infarction of the European Society of Cardiology (ESC). ESC Guidelines for the Management of acute myocardial infarction in patients presenting with ST-segment elevation. Eur Heart J. 2012;33(15):2-51.

4. O'Gara PT, Kushner FG, Ascheim DD, Casey DE Jr, Chung MK, de Lemos JA, et al; American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction: a report of the American College of Cardiology Foundation / American Heart Association Task Force on Practice Guidelines. Circulation. 2013;127(4):e-362-425.

5. Goldstein P, Wiel E. Management of prehospital thrombolytic therapy in ST segment elevation acute coronary syndrome (<12 hours). Minerva Anestesiol. 2005;71(6):297-302.

6. El Khoury C, Sibellas F, Bonnefoy E. Is There Still A Role For Fibrinolysis in ST-elevation myocardial infarction? Curr Treat Options Cardiovasc Med. 2013;15(1):41-60.