

SPECIAL COMMUNICATION

SUPPORT WITH CLARITY: A PROPER TREND IN MEDICAL STATISTICS

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(The analysis of Past JAMC articles has been used purely for academic purposes and authors intention is not to criticize any work)

Background: The aim of this study was to establish effective methods to review and evaluate, and to emphasize in support with clarity as a proper trend in medical statistics. **Methods:** The clinical research material used in this study is stemmed from JAMC. Study:I, N is 220 subjects, from Pattern of Coronary Arterial Distribution and Its Relation to Coronary Artery Diameter, Z A Kaimkhani, MM Ali, AMA Faruqi JAMC Jan-Mar 2005; 17(1): 40-3.¹ Study:II, N is 105 patients, from Sclerotherapy Plus Octreotide Versus Sclerotherapy Alone In The Management Of Gastro-Oesophageal Variceal Hemorrhage. HA Shah, K Mumtaz, W Jafri, S Abid, S Hamid, A Ahmad, Z Abbas. JAMC Jan-Mar 2005; 17(1): 10-4. ² Systemic review and evaluation with statistical principles is to be used. **Assessment and discussion:** The reports of 2 clinical researches from JAMC are assessed, and both used for demonstrating the characteristics and pitfalls statistically. **Conclusion:** Before reaching any significant difference in statistics, hopefully, all clinicians will be able to deal with the data to be measured by selecting proper statistical models as the best as we can in order to gain appropriate inference in medical statistics.

Key words: Regression, prediction, correlation, survival, variable

INTRODUCTION

In general speaking, there are two commonly used methods in statistics for describing relationship between two (sets of) variables: a correlation study and a regression analysis. It is not always both can be used for prediction. Regression analysis is certainly a preferred and more definitive one. After all, there is some difference between these two methods.

The logistic regression model is not really a prediction model. It models the chance of success in terms of the predictors x_1, \dots, x_k .

But for a given individual with predictor values x_1, \dots, x_k , all we can do is calculate her chance of a success, and to ascertain that $F(b_0 + b_1*x_1 + \dots + b_k*x_k)$ is close to zero or one, so that our "prediction" will be very reliable.

MATERIAL AND METHODS

The clinical research material used in this study is stemmed from JAMC 2005 volume 17 issue 1.

Study: I, N is 220 subjects, from Pattern of Coronary Arterial Distribution and Its Relation to Coronary Artery Diameter ZA Kaimkhani, MM Ali, AMA Faruqi. JAMC Jan-Mar 2005; 17(1): 40-3.¹ and Study:II, N is 105 patients, from Sclerotherapy Plus Octreotide Versus Sclerotherapy Alone In The Management Of Gastro-Oesophageal Variceal Hemorrhage. HA Shah, K Mumtaz, W Jafri, S Abid, S Hamid, A Ahmad, Z Abbas. JAMC Jan-Mar 2005; 17(1): 10-4.²

The approach set out in this article not only use medical statistic principles and methodology, but also emphasize the importance of being systematic.

ASSESSMENT AND DISCUSSION

Age

Age is a potential predictor, so far as patients' outcome concerned. The conclusion might be very different if age is important but omitted from the model. This seems not like any important issue in the study II, since for the sclerotherapy+Octreotide is 49.5 ± 14.2 years old in age, and for the sclerotherapy alone group, it is 50 ± 12.3 years old. On the other hand, for the study I, the age was reported as mean of 50 ± 9.6 years old.

The interaction between 2 independent variables

In study II, the means with standard deviations of age are as stated, while the 'Logistic regression analysis, incorporating all the characteristics in table 1 indicated that the factors independently associated with survival without rebleeding at 5 days were the treatment assigned ($p=0.002$) and the presence of active esophageal variceal bleeding ($p=0.02$).¹ 2-p. 12-3

Had age and each of [the treatment assigned] variables been dichotomized according to their respective means, the associations between all independent variables been computed as odds ratios (OR) and 95% confidence intervals, three-way cross-tabulations of patients' outcome, age, and an independent variable been computed, Breslow-Day³ test been performed to determine homogeneity of the

treatment variables' odds ratios across age strata, and Mantel-Haenszel summary odds ratios and 95% confidence intervals been computed, a multiple logistic regression models been used for simultaneous consideration of age, active bleeding, and a treatment variable, these models been computed with the Epidemiological Graphics, Estimation, and Testing package⁴ in order to investigate the combined effects of 2 variables, namely, active bleeding and treatments on patients' outcomes, and a logistic models been computed with the following two sets of models:

- 1) age + [the presence of active esophageal variceal bleeding] + the treatment assigned] this set of models investigate the independent effects of [the presence of active esophageal variceal bleeding], and [the treatment assigned],
- 2) age + [the presence of active esophageal variceal bleeding] + [the treatment assigned] + the product after multiplication of both, this set of models examine the independent effects of [the presence of active esophageal variceal bleeding], [the treatment assigned], and the product of both; therefore, these would have shown the variable of Interaction^{3, 25} between 2 original independent variables, namely, [the treatment assigned (p=0.002)], and [the presence of active esophageal variceal bleeding (p=0.02)].

This new independent variable is the product of the other 2 aforementioned original independent variables, that is Interaction= [the treatment assigned (p=0.002)] x [the presence of active esophageal variceal bleeding (p=0.02)], while these 2 original variables must be either continuous or binary data, which is consistent with the situation in Study II.

Wherever and whenever there is an interaction between variables, there must be confounding effect.^{6,7} One of the main purposes of applying Multivariate analysis is trying to control confounding factors.⁶⁻⁸ The way to eliminate interaction is to have both forward and stepwise selection in the multivariate analysis. With regard to the significance of the p value of Interaction, it will be discussed in upcoming section.

A significant p value

Whenever a clinical picture indicates a patient has no disease, just as a positive diagnostic test does not mean otherwise, a significant p value does not mean that a clinical research hypothesis is accurate, especially if it is not consistent with any current medical and /or public health knowledge.⁸

In Study II, had the Interaction of 2 independent variable been taken into account, the new p values, if any, of variables [the treatment assigned (p=0.002)], [the presence of active esophageal variceal bleeding (p=0.02)], and now even including that of Interaction, would have been all very low, and much less than the commonly used alpha= 0.05. Why the newly obtained significant p values are so much less than 0.05? It is indirectly self-evident that Interaction does exist! Under such a circumstance, one will encounter the difficulty in interpreting p values of the original 2 independent variable: [the treatment assigned], and [the presence of active esophageal variceal bleeding], namely p=0.002, and p=0.02 respectively. Therefore, it requires stratification of the original data.

The influence of missing data upon sample size

One of the other explanation for such a low p values, which likely such a possibility will be remote in the case of Study II, is the influence of missing data in one, or some, and/or even all of the groups. As in Study II, among the total 105 patients, all “ adult patients admitted to the AKUH with a history of hematemesis or melena (or both) within 24 hours prior to admission were evaluated. Cirrhosis of the liver had either been diagnosed previously or on current admission on the basis of clinical signs of chronic liver disease such as ascites, palmar erythema, spider angiomas, splenomegaly and biochemical evidence of derangement of liver function, abdominal ultrasound and / or liver biopsy where possible.”^{2-p.11} Therefore, data has hopefully been well kept, for which, the authors can be trusted. Academically speaking, why the effect of missing data can influence such low p values, as low as p=0.002, and p=0.02 in Study II? As in handling in multivariate analysis, the computer software¹⁰ requires that all the variables must have intact and complete observed values prior to its starting the job. Therefore, for those samples, which have had missing data, the sample size will be automatically reduced by the software. Consequently, the mean survival time of various groups with treatments assigned will be remarkably diminished upon Multivariate analysis!¹¹⁻¹³

The distribution of samples

With respect to the independent variable, such as in both Study I and II, in fact, a correlation tree to check for any relation between (and / or among) each independent variables may be helpful. For example in Study I, there appears no clear indication on whether the sample is on normal distribution or not. While on its page 4, the first paragraph stated that '

Table 4 shows the correlation between coronary artery distribution and their diameters.', whereas the title of the said table, which is indicated on the very same page, (just above the said table per se), states as 'Comparison of Mean Coronary Artery Diameter (mm) in relation with the Coronary Artery Dominance pattern'.^{1-p. 42} In fact, it appears to be neither correlation, nor comparison statistically, but seems merely representing an observation about mean diameter of coronary arteries in different pattern of distribution anatomically, more specifically, with regard to its right, left, or co-dominant patterns. Statistically speaking, whether the sample from Study I is in a normal distribution or not is important to be ascertained, prior to any one can really address to any correlation of data, not only in Study I, but also in any other researches. Had the data of Study I been plotted on a graph, and had it been shown a non-normal distribution, that would have shown likely positively skewed. If in reality this is the case, then it will be more appropriate to use a nonparametric test on the data set.

The assumption of statistical hypothesis

Although each statistical test (method) does require its assumption as null hypothesis, unfortunately there have been some published results of clinical trials that had violated such statistical assumptions.¹⁴⁻¹⁸

As to the test group differences, Chi square (13-14, 18, 19), Kruskal-Wallis (this test has no statistical assumption that the samples/populations are in normal distribution), and ANOVA tests are to be used.

In Cox regression model, which is a commonly used tool among all the multivariate survival analysis.^{9, 21}, there is a statistical assumption to reduce the proportional hazard. Furthermore, this assumption to reduce hazard is across all the time, regardless at first 48 hours after a bleeding, survival without rebleeding at 5 days (such as in the case of Study II), one month, 3 years, or even more than 3 years after treatments.

Before researchers infer any significance of the p values, and other values of coefficient, it is also advisable to do such tests for the statistical assumption.²⁰⁻²⁴

CONCLUSION

From a systemic approach in medical statistics to codify the best way in solving clinical and public health research problems, there is really no any easy job to do. Technically and frankly speaking, there is no solitary way that will be able to please every party involved. Indeed, this approach will seem somewhat viewed through the rose-tint glasses, as the real world of clinical and public health research would be

more chance and random than those have been delineated as aforementioned. In summary, in this article, two reports of clinical researches from JAMC were used for illustrating the distinctiveness and drawbacks in medical statistics, with emphasis stressed upon regression and correlation. Instead of criticism as "Support versus illumination: trends in medical statistics." in the 1980s¹⁴⁻¹⁶, herewith as aforementioned, we have sincerely expressed the importance of supports cordially with clarity, and it will certainly be the proper trend of practice in medical statistics in these days of 2006. Therefore, before reaching any significant difference in statistics, hopefully, all clinicians will be able to pay attention to nature of data, influence on sample size, the significance of p values, the possible existence of interaction^{4, 5, 25} between variables, and the assumption of statistical hypothesis²²⁻²⁴ per se.

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REFERENCES

1. Kaimkhani ZA, Ali MM, Faruqi AMA: Pattern of Coronary Arterial Distribution and Its Relation to Coronary Artery Diameter. J Ayub Med Coll Abbottbad 2005; 17(1):40-43.
2. Shah HA, Mumtaz K, Jafri W, Abid S, Hamid S, Ahmad A, Abbas Z: sclerotherapy plus octreotide versus sclerotherapy alone in the management of gastroesophageal variceal hemorrhage . J Ayub Med Coll Abbottabad 2005;17(1):10-14.
5. Breslow NE, Day NE, Davis, W: Statistical methods in cancer Resaerch. International Agency for Research on Cancer, 1980. iAH Iterface de pesquisa 2.5.4.
6. Epidemiological Graphics, Estimation, and Testing package. Cytel Software Corporation: Egret References Manual. Seattle, WA, 1985-1990.
7. Browner WS, Newman T B: Are all significant p values created equal? JAMA May 1987;257(18):2459-2463.
8. Dixon WJ (ed): BMDP Statistical Software Manual. Berkeley, University of Livonia Press, 1990;2:873-889.
9. Schlesselmam JJ: Case-control study: Design, Conduct, Analysis. New York, Oxford University Press, 1982:58-62.
10. Fleiss JL: Statistical method for Rates and Proportions. 2nd ed., John Wiley & Sons, New York, 1981:177-178
11. Miller RG. Survival Analysis. 1st ed., John Wiley & Sons, New York, 1981:96-98.
12. SAS/STAT User's Guide. Gary. SAS Instit Inc, 1990;1:105-108.

13. Lee ET, Wang J W: Statistical Methods for Survival Data Analysis. John Wiley and Sons, 1st ed. Hoboken, N J, 1980:76-87.
14. Lo SK, Li I, Tsou T, See L: Non-significant in Univariate but Significant in Multivariate analysis. *Chang Gung Med J* June 1966;18(2):95-101.
15. McKinney WP, Young MJ, Hartz A: The inexact use of Fisher exact test in six major medical journals. *JAMA* 1989;262:3129.
16. Katz DL: Clinical epidemiology and evidence-based medicine: fundamental principles of clinical reasoning and research. London 1st ed. Sage 2001:147-79.
17. Longnecker DE: Support versus illumination: trends in medical statistics. *Anesthes* 1982;57:73-4
18. Ohnhaus EE, Adler R: Methodological problems in the measurement of pain: a comparison between the verbal rating scale and the visual analogue scale. *Pain* 1975;1:379-84.
19. Wassertheil-Smoller S. Biostatistics and epidemiology: a primer for health professionals. 2nd ed. Berlin: Springer-Verlag, 1995:139-40.
20. Berger VW: Improving the information content of categorical clinical trial endpoints. *Control Clinical Trials* 2002;23:502-14.
21. Rich H, Luby AL, Babikan HM: Misuse of the Chi square test. *Lancet* 1974;7869:1294-5.
22. Armitage P, Colton T: Encyclopedia of Biostatistics, John Wiley & Sons, 1st ed. New York, 1998.
23. Cox DR, Oakes D: Analysis of Survival Data, Chapman & Hall, New York 1984
24. Lawless, J.F. Statistical Models and Methods for Lifetime Data, John Wiley & Sons, 1st ed., New York, 1982.
25. Marthens D, Farewell, VT: Using and Understanding Medical Statistics, Karger, 1st ed., New York, 1996.
26. Woolson RF, Clark, WR: Statistical Methods for the Analysis of Biomedical Data, John Wiley & Sons, 2nd ed. New York, 2002.
27. Hall EM, Johnson JV, Tsou TS: Women, occupation, and Risk of Cardiovascular Morbidity and Mortality. *Occupational Medicine* 1993;8:709-719.

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