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Analysis by Categorizing or Dichotomizing Continuous Variables Is Inadvisable: An Example from the Natural History of Unruptured Aneurysms

SUMMARY: In medical research analyses, continuous variables are often converted into categorical variables by grouping values into ≥ 2 categories. The simplicity achieved by creating ≥ 2 artificial groups has a cost: Grouping may create rather than avoid problems. In particular, dichotomization leads to a considerable loss of power and incomplete correction for confounding factors. The use of data-derived "optimal" cut-points can lead to serious bias and should at least be tested on independent observations to assess their validity. Both problems are illustrated by the way the results of a registry on unruptured intracranial aneurysms are commonly used. Extreme caution should restrict the application of such results to clinical decision-making. Categorization of continuous data, especially dichotomization, is unnecessary for statistical analysis. Continuous explanatory variables should be left alone in statistical models.

ABBREVIATIONS: ACA = anterior cerebral artery; CHUM = Centre hospitalier de l'Université de Montréal; ICA = internal carotid artery; ISUIA = International Study of Unruptured Intracranial Aneurysms; MCA = middle cerebral artery; Pcirc = posterior circulation; PcomA = posterior communicating artery; SAH = subarachnoid hemorrhage; UIA = unruptured intracranial aneurysms

UIAs are common (approximately 2% of the adult population), but they most often remain silent until a rupture occurs (incidence, 2–20/10,000/year).¹ No one is sure what to do with them, but with the increasing accessibility of noninvasive imaging of the brain, the problem is growing rapidly.²

A common and yet controversial approach to decision-making is to compare the natural history of the disease and the risks of treatment.^{3,4} One prominent risk factor for rupture of UIAs is size. In 1998, a landmark study on this subject, the ISUIA, estimated from retrospectively obtained data that the risk of rupture of aneurysms smaller than 10 mm was extremely low.⁵ Subsequent guidelines published in 2000 discouraged the treatment of aneurysms smaller than that size.⁶ In a 2003 study, the same group, confronted with different results when data were collected prospectively, claimed that aneurysms < 7 mm in a special subgroup of patients (defined by the absence of a history of rupture of another lesion, having an aneurysm located in the anterior circulation, and selected for observation) were at zero risk of rupture, but only when some carotid aneurysms were excluded (PcomA aneurysms).⁷ Despite these specifications, a threshold of 7 mm is now used

by many as a normative criterion for clinical decisions⁸ or in cost-effectiveness analyses.⁹

Size of UIAs can serve to illustrate the problems associated with the categorization of continuous variables, in particular dichotomization. Our aim is to consider how continuous variables should be treated and analyzed when we suspect that risk increases or decreases in proportion to the variable in question. We address the following questions: What are the advantages and disadvantages of categorization? If we determine a size threshold in a data-dependent fashion, how reliable are the results? Is the methodology presented in the ISUIA study⁷ sufficiently reliable to serve as a basis for clinical decisions? Finally, we discuss more appropriate ways of analyzing continuous variables in clinical research.

Categorizing Continuous Variables

Measurements of continuous variables are made in all fields of medicine. Common examples include blood pressure, respiratory function, age, body mass index, and the size of a lesion. They are often converted into categorical variables by grouping values into ≥ 2 categories. For example, high blood pressure is defined as a systolic pressure of 140 mm Hg or higher and/or a diastolic pressure of 90 mm Hg or higher; an adult who has a body mass index of 30 or higher is considered obese. Categorization of continuous variables makes the analysis and interpretation of results simple: It is easy to understand what was done and what the results are, and it spares us the need for assumptions about the nature of the relation between the variable and the outcome or risk. Furthermore, clinical decision-making often requires 2 classes, such as normal/abnormal, risky/benign, treat/do not treat, and so on. However, dichotomization has many drawbacks and is widely criticized by statisticians.^{10–15} What is necessary or sensible in clinical and therapeutic settings is not relevant to how research data should best be analyzed. Indeed, in the clinical research context, such simplicity is gained at a high cost and may well create problems rather than solve them. Difficulties associated with the treat-

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Five-year aneurysm cumulative rupture rate^a

	Aneurysms <7 mm		Aneurysms 7–12 mm	Aneurysms 13–24 mm	Aneurysms >25 mm
	Group 1 ^b	Group 2 ^c			
ACA/MCA/ICA	0	1.5%	2.6%	14.5%	40%
Pcirc/PcomA	2.5%	3.4%	14.5%	18.4%	50%

^a Data from Wiebers et al.⁷^b Patients who had no prior history of aneurysmal SAH.^c Patients who had a prior history of aneurysmal SAH.

ment of continuous variables arise very widely across the spectrum of medical and surgical specialties. We will illustrate these issues by using the case of UIAs as assessed in the second ISUIA study.⁷

How Size Was Analyzed in the Prospective ISUIA Study

The prospective ISUIA study⁷ is a significant example in our field. This study represents the most important contribution to the knowledge of the elusive natural history of UIAs to date. Published in 2003, it included 4060 patients enrolled during a 7-year period from 60 centers in the United States, Canada, and Europe. Multiple categories of patients and aneurysms were created according to clinical history, size, location of aneurysms, and management of patients. The 4060 patients studied included 983 who had a history of aneurysmal SAH (group 2) and 3077 without such a history (group 1). A total of 2368 patients were treated, 1917 by clipping and 451 by endovascular therapy, while 1692, who did not have aneurysm treatment, were considered the “natural history group” and will be the target of the current discussion. There were 2686 aneurysms in these 1692 patients; 40% of patients had multiple aneurysms. It is unclear how patients were categorized and how eventual ruptures were allocated when patients had multiple aneurysms because categories concern patients, but size is a characteristic of aneurysms. We can only presume that the largest of multiple aneurysms, along with its location, served to categorize the patient, at least in Table 4 (which seems to add up for patients, not for aneurysms).⁷ There is room here for different interpretations.

The hypothesis in the ISUIA study was that size was an important risk factor for future ruptures. One must at first consider the uncertainty of measurements, the imprecision of the methods of correction for magnification and for various projections, from imaging studies performed between 1991 and 1998 from multiple institutions with diverse equipment of widely ranging quality. Patients who were observed were selected according to clinical judgment, and it is fair to assume that this decision was partly based on the variable to be studied: size. Hence not only are the observations biased but they cannot be representative of the natural history of patients whom physicians want to treat.

In the ISUIA study, the resulting group of patients left untreated was divided into 4 size categories as seen in the Table. Categories of sizes were determined in a data-dependent fashion: “the running average for successive 3-mm-size categories showed optimum cut-points at diameters <7 mm, 7–12 mm, 13–24 mm, and 25 mm or larger”⁷ for the 5-year cumulative rupture rates, illustrated in Table 4 but grouped in 3 categories (≤ 7 , 7–12, and > 12) for the multivariate analyses of predictors of hemorrhage. The 3 categories further changed for clinical outcomes 1 year after treatment: Here the categories were

≤ 12 , 13–24, and > 25 . It is unclear how and why groupings were constructed or dismantled because sometimes the size categories were split according to the previous history of the patients (group 1 or 2 for aneurysms <7 mm) and sometimes they were lumped (> 7 mm). The same problem resurfaces when location is considered a characteristic to be used for categorizing in combination with size, with the further problem that some anatomic locations are unorthodox (with some carotid aneurysms that have presented an event, the PcomA, now being lumped with the posterior circulation aneurysms). Remember that these problems are compounded by the fact that 40% of patients had multiple aneurysms of various sizes and locations.

It remains impossible to work out precise numbers because they are not provided in Table 4, which included only percentages.⁷ It is even unclear if we are here dealing with actual events or estimated events because Table 4 presented 5-year cumulative percentages, while the mean follow-up period was 4 years.⁷ At least 15 different categories are presented in Table 4 (and probably 3 times as many have been played with), while there were only 49 (or 51) events, far too few to provide any confidence in the attribution of risks to any individual category.⁷ Confidence intervals cannot be calculated because precise numbers were not provided, but they must be very wide. If rates deprived of confidence intervals are then projected over the lifetime of an individual to provide a natural history or prognosis, with the presumption that risk remains constant, incalculable error is multiplied beyond control. Even if ISUIA 2003 did not explicitly use 2 groups split at 7 mm—the authors never gave the overall rupture rate for <7 mm aneurysms—the 5-year cumulative rupture rates rise above 7 mm for all locations. Consequently many clinicians now use the 7-mm limit as a threshold to guide clinical decisions. Multiple methodologic flaws are involved in this conclusion, which is, in our opinion, unjustified and risky, but our discussion will be restricted to categorization of continuous data.

Problems with Dichotomization

The first problem that categorizing a continuous variable causes is loss of information; that loss is small with several groups and is most severe with just 2 groups. Several studies^{16,17} have demonstrated that 100 continuous observations are statistically equivalent to at least 157 dichotomized observations. Selvin¹⁸ derives a formula to calculate the efficiency loss due to categorizing a continuous variable. The problem increases in importance when one attempts to take into account confounding factors to reveal the relation between the event rate and the variable. Becher et al¹⁹ found that models with a categorized exposure variable removed only 67% of the confounding controlled when the continuous version of the variable was used. A further important disadvantage of dichot-

omization is that it does not make use of within-category information: Everyone above or below the cut-point (often the sample median) is treated as equal, yet their prognosis may vary considerably. Dichotomization by necessity leads to pooling groups with different risks and to an unrealistic “step function” for risk. The risk of misclassification because of measurement error is high. In addition, comparing studies that used different cut-points becomes impossible. Hence, for most statisticians, dichotomization is not a natural way of analyzing continuous data.

In the ISUIA, the cut-points were chosen after inspecting the data, rendering all results exploratory and in need of confirmation from data of a different source before being seriously considered for clinical decisions. If size is to be dichotomized, the choice of a cut-point should be made before analysis and, if possible, with some theoretic or clinical justification. The size of the *P* value or odds ratio should never influence the choice of cut-points.²⁰ This procedure leads to *P* values that are too small and overestimates the prognostic value of the variable.

Some researchers have argued that loss of power and efficiency is not important if statistically significant effects are still found with dichotomous variables.^{21,22} Why should we use a regression coefficient, a concept the meaning of which may be less likely to be understood by typical research consumers? Indeed, if type I and II errors are all that matter and the results achieve statistical significance, researchers might feel justified in dichotomizing such measures so as to simplify conclusions. The objective of such research should be to get reliable estimates of risk, not just to ensure a statistically significant result. What is not well appreciated in this reasoning is that categorizing continuous variables may not only miss the message, it can also get it wrong: Under some circumstances, categorizing continuous variables can give biased results. In a simulation study, Taylor and Yu²³ found that categorizing 1 continuous variable can artificially make another variable appear associated with the outcome. More generally, the cut-point chosen by looking into data during the categorization of continuous variables significantly changed the calculated odds ratio.^{10,18,24} Information loss and bias from categorizing continuous variables explain why statisticians frequently warn us to leave continuous variables alone.

There is thus much support for using regression analysis in which variables are kept continuous. Although this approach is simplest when there is a reasonably linear relation between the variable and the outcome, it is not difficult to extend the approach to nonlinear relations.¹⁰ It appears that this advice was lost to investigators—ourselves included—who have developed risk stratification schemes for patients with UIAs. Most rupture-risk stratification schemes have categorized size by using arbitrary or data-driven cut-points. Much the same practices have been documented in other areas,^{25–28} so it is clear that the many warnings by statisticians against this type of analysis have not been heeded.

Conclusions and Recommendations

Forcing individuals into 2 groups, such as <7 mm and ≥7 mm, is widely perceived to simplify analyses and facilitate presentation and interpretation of findings. In fact, size is so frequently dichotomized that some may believe this to be a rec-

ommended practice. Use of categories yields results that are readily understood by colleagues, policy makers, and the interested public. Nevertheless such results may distort the reported relationship and poison the clinical meaning of findings. Modern regression models do not require categorization. In general, continuous variables should remain continuous in regression models designed to study the effects of the variable on the outcome of interest.

We recommend the following:

- 1) If a continuous variable such as size is to be dichotomized, the choice of cut-point should be made before analysis and with some theoretic or clinical justification. Data-driven cut-points should be avoided. Never choose an optimal cut-point based on minimizing the *P* value or maximizing statistics such as odds ratios.
- 2) If a continuous variable is categorized, having ≥3 groups is preferable to just 2. Again, prespecification of cut-points is strongly recommended.
- 3) If the assumption of a linear relation (eg, between rupture risk and size) is supported, size can best be used as a continuous variable in a regression model. Careful interpretation of the resulting odds ratio as representing the effect for each additional millimeter can be readily understood by readers. Nonlinear relations can also be quite easily modeled.^{29,30}

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