Multilevel data analysis: What? Why? How?

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Central Message

Multilevel data structure is observed frequently in cardiac surgery studies. Mixed-effects modeling is the most appropriate way to analyze such data, with readily available software.

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Parolari and colleagues¹ report a prospective study of variables associated with arterial and venous coronary artery bypass graft occlusion by computed tomographic angiography 15 to 21 months after surgery, with a focus on D-dimer elaboration after surgery. They imaged 503 grafts in 179 patients. To the average reader, data analysis should be simple: count the occluded grafts, divide by 503 to obtain the proportion occluded (perhaps expressed as a percentage), then use logistic regression analysis to identify risk factors for occlusion. Instead, the reader is met with unfamiliar terms such as “mixed model” logistic regression. What is going on?

On closer reflection, the reader comes to realize that each patient had, on average, 3 grafts. All 3 were exposed to the same D-dimer levels and other individual patient variables. This means that grafts in a given patient are not completely independent of each other. How do we sort this out? This is a challenge we face daily as reviewers for this *Journal*, and something with which the authors had to contend.

For this commentary, we will call such data “multilevel data”—graft-level and patient-level—that requires an analysis that accounts for its multilevel structure.

WHAT?

In many clinical studies, data are naturally multilevel (“nested”). The data of Parolari and colleagues¹ have a 2-level structure. Consider a more complex study of patient-experience data. Individual patient responses are nested within different nursing units, which are nested within different hospitals (Figure 1), a 3-level data structure. This nesting could be further extended to hospitals within different systems, within different geographic regions—data with a hierarchical structure.^{2,3} Other frequently encountered multilevel data structures include

FIGURE 1. Multilevel data structure for patient-experience data.

FIGURE 2. Multilevel data structure for coronary artery bypass graft patency data.

repeated measurements of spirometry after lung transplant, also a 2-level data structure,⁴ or coronary bypass graft stenosis measured at different time points, nested within different grafts, with graft types nested within a patient (Figure 2), a 3-level data structure. Importantly, concomitant information (potential risk factors or modulating factors) may be available at each nested level. Thus, in patient-experience data (Figure 1), one may have patient-level data (eg, age), nursing unit-level data (eg, nurse-patient ratio), and hospital-level data (eg, teaching hospital).

WHY?

Ordinary regression models assume observations are independent. However, nested observations tend to be correlated at each level, because lower-level observations share common groupings at higher levels. Failure to take these correlations into account may lead to biased estimates. Parolari and colleagues¹ assessed the effect on graft patency of concomitant information from both levels, patient and graft.

HOW?

As we tell authors, proper analysis of multilevel data requires collaboration with a statistician knowledgeable in mixed-effect models or longitudinal data analysis. The language of these analyses is generally unfamiliar. What is

“mixed?” Specific variables at each level, often constant across groups in a level, are called “fixed effects”; variables related to hierarchical levels themselves, often individually identified patients as in Parolari and colleagues,¹ are called “random effects.” Thus, “mixed effects” statistical models sort out effects at each data level.

Although we direct investigators to software for such analyses (PROC NL MIXED SAS, aML,⁵ HML, MLwiN⁶), this field of statistics is developing rapidly and advancing. We need to be aware of it, but we also need experts to perform the analyses and interpret the results.

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