

## Is Postoperative Cognitive Decline Clinically Relevant?

To the Editor:

We applaud Avidan *et al.*<sup>1</sup> in their assessment of the general relationship between postoperative cognitive dysfunction (POCD) and dementing illness. We have a number of questions and concerns, and we hope the authors might address them.

As noted by the authors, the report revisits the question of whether geriatric patients who undergo surgery have a more rapid decline into dementia than patients who do not have surgery. However, our interest as physicians may be better stated as examining whether POCD is clinically relevant. Previously, large studies of POCD in noncardiac surgery have shown an incidence of approximately 10% at 3 months.<sup>2,3</sup> Williams-Russo *et al.*<sup>4</sup> reported a rate of approximately 5% at 6 months, whereas the long-term follow-up of international study on POCD found a difference of approximately 1% from the control patients.<sup>5</sup> It has been already established that most patients seem to recover, albeit over a prolonged period of time. Given their negative finding, it would be helpful if the authors could provide some insight into the statistical power of their advanced statistical approach. Because the relationship of the testing sessions in the Alzheimer's Disease Research Center group to the events in question is highly variable and the incidence of POCD decreases over time, a clear statement of the statistical power of study is critical to understand the importance of the current report. We suspect that the study may have been underpowered because of the limited number of major surgical procedures in the sample. We would predict that one would have to examine more than 6,700 patient records per group to detect a 1% difference at 1 yr. In any case, we do not agree that cognitive effects that last less than 1 yr are clinically unimportant and therefore question the authors' advice that "The decision to proceed with surgery in elderly people, including those with early Alzheimer disease, may be made without factoring in the specter of persistent cognitive deterioration." Three or 6 months of cognitive deterioration may indeed profoundly impair quality of life and have significant socioeconomic consequences.

The importance of the preoperative trajectory has not been discussed in most reports of POCD, but it is an extremely interesting idea that the authors might develop further. As most patients in the United States are scheduled for surgery within at most a few months of their procedure, would testing at that point be more relevant? If the type of testing suggested by the author's analysis would be clinically

impractical, does the current data set provide data regarding the magnitude of the issue and some insight on how to compensate appropriately?

Although the authors note the well-known controversies regarding what standard should be used to define POCD, the majority of the POCD literature has defined POCD through cognitive testing of specific areas, generally memory and executive function. In this article, the authors use an instrument to define dementia: the Clinical Dementia Rating Scale. Dementia, as rated by the Clinical Dementia Rating, is a much broader concept that includes assessment of community affairs, home and hobbies, and personal care in addition to psychometric alterations. The authors do not present a rationale for suggesting that marked alteration in the Clinical Dementia Rating at 1 yr is more, or less, compelling than the methodologies used by previous studies. Although this scale does provide an important link to dementia research, it will be difficult to compare the current result with majority of the literature published to date.

It is difficult to understand the nature of the simulated event that defines the control group in this study. If these are the controls, then they are all preevents; therefore, it would be helpful to understand how the simulated event was determined. Was the process one of simply selecting a date that was called an event, with determinations then falling before and after? What impact does the selection of the simulated events have on the subsequent outcome? What is the interpretation of a change in slope after an event that did not actually occur?

The authors bring up a number of serious concerns about control groups and their relevance to the definition of POCD. We agree with the authors' concerns regarding the constitution of an appropriate control group. However, we do not understand how the current analysis provides evidence that such control groups are unnecessary in prospective clinical studies.

The authors restrict inclusion criteria to those with a postevent observation. This inclusion criterion will result in a potential bias in the postevent estimates, because the analytic model assumes that those who died or were lost to follow-up have the same trajectories as those who remain under follow-up. A joint effects model<sup>6</sup> that would include not only the cognitive trajectories but also the survival curves may result in unbiased estimates. However, because the proportion of subjects who died during follow-up within each group is not reported, the readers cannot determine whether deaths differentially occurred.

The authors acknowledge a skewed distribution in the number of observations preevent and postevent for the surgical and illness groups but did not find these statistically significant. The important difference may be that the illness group had a median 1.3 more annual preevent

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observations to contribute to their slope estimate. For POCD, one would expect that postevent decline was greatly close to the event. The illness group had a median difference of 1.7 fewer annual postevent measures contributing to their slope estimate. As these preevent and postevent measures are linear and marginal, it is conceivable that having a different number of observations preevent and postevent could mask important differences.

Once again, we applaud the investigators' effort to facilitate our understanding of this information.

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## Cognitive Decline in Older Subjects

To the Editor:

Avidan *et al.*<sup>1</sup> have taken on the difficult task of looking through the vast Alzheimer's Disease Research Center database to clarify the effect of noncardiac surgery on the progression of Alzheimer's disease and age-matched controls. Alzheimer's disease is a long-term condition of progressive cognitive deterioration of unknown etiology, with widely accepted pathologic markers.<sup>2</sup> It is not surprising that single episodes of various medical illnesses, surgery, and anesthetic techniques cannot be shown to alter its course, as the authors rightly conclude. However, we think that the lack of observed effect, reported in the 214 nondemented participants, warrants further scrutiny.

As in previous studies,<sup>3,4</sup> the authors have based their conclusions on a composite score, derived from a battery of neuropsychological tests. In one previous study to which the authors refer, tests were selected by the investigators, based on their "appropriateness." The cognitive tests used in the present study are those selected for tracking the functional changes of Alzheimer's disease. In either case, tests to identify or dismiss any cognitive deficit resulting from anesthesia or surgery have not been systematically sought.

Testing in the current study has been performed at different intervals, after a variety of operations or illnesses, and different numbers of tests were performed on the participants, all included in the calculated slopes, which are the basis for their conclusions. The authors also agree that the testing was skewed, in that a relatively small number of participants underwent multiple testing. This pool of heterogeneous data limits the impact of the study. Given the wide range of illnesses, operations, follow-up intervals, numbers of tests, *etc.*, we wonder why the authors have chosen not to provide the data for individual tests, follow-up intervals, or data plots to support their conclusions.

In addition, the collection of postevent data differs with mean values of 1.2 or 2.1 yr (illness and surgery groups, respectively). Is it acceptable for a patient to have postoperative cognitive dysfunction for a median of 2.1 yr after surgery, provided they (eventually) resume their existing level of decline in cognitive function? It also leads us to question the authors' headline conclusion that "The decision to proceed with surgery in elderly people, including those with early Alzheimer's disease, may be made without factoring in the spectre of persistent cognitive deterioration." This is not only an unacceptable conclusion but may also hinder future interest and research in an area that the authors themselves accept is of great importance!

This is a retrospective report, and the authors have not designed the study to answer their question directly. Collection of data at intervals to reproduce the transient cognitive defect found in the early postoperative phase (reported by Moller *et al.*), followed by the absence of a long-term deficit, would have been compelling support for the authors' hypothesis. We hope that the authors will use the resources of their Alzheimer's Disease Centre to perform a prospective study, designed to delineate the effect of anesthesia and surgery on cognitive function in this age group.

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