

Outcome Measures for PCO Studies

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The candidate outcome measures for studies of posterior capsular opacification (PCO) may be placed into four categories: visual measures, clinician grading, image analysis, and surgical outcomes. I will discuss the advantages and disadvantages of each approach.

Visual Measures

One of our primary considerations should be what the patient sees. In this regard, visual acuity should be measured using logMAR charts and scored by letter correct.^{1, 2} This approach would allow visual acuity to be treated as a continuous variable (or interval scale). The data may then also be treated as categorical by considering the number of patients that lose 2 or more lines of visual acuity (10 letters or 0.2 logMAR).

Some vision scientists might argue that visual acuity is not a "sensitive" enough measure and that alternative tests should be used, such as contrast sensitivity and glare.³ This assertion is supported by Tan *et al.* who found that PCO affected Pelli-Robson contrast sensitivity by 0.29 log units but only reduced visual acuity by 0.15 log units.⁴ Their data on disability glare assessment are less convincing. Sponsors may be able to collect useful information with these supplementary techniques, but should use tests whose repeatability has been established³ and whose outcomes can be translated into clear language in product labeling.

The primary disadvantage of visual assessment is that we are dealing with an aging population that is susceptible to reductions in vision that are unrelated to PCO. In a randomized clinical trial, patients in treatment and control groups would presumably be equally susceptible, but study design and sample size considerations should take this into account.

Clinician Grading

Standardized photographic scales are available for grading cataract, e.g. LOCS III.⁵ To my knowledge no widely accepted standards have been published for the grading of PCO. I would argue that clinician grading of PCO should not be used unless a valid and repeatable system has been developed that includes photographic standards and not just verbal descriptors. A limitation of using subjective grading systems is the potential for clinician bias. Masking of clinicians would be desirable but may not be feasible if the IOLs under study have distinctive features.

A potentially useful variant of subjective grading is the development of a PCO reading center. Slit-lamp photographs could be taken using established protocols and sent to a reading center. The photos could then be graded by trained and masked readers. Concentric circles could be superimposed on the photographs so that different regions of the capsule could be graded separately.

Image Analysis

A number of researchers have developed sophisticated image capture and analysis systems.⁶⁻⁹ Others have employed the Lens Opacity Meter.¹⁰ My impression is that retro-illuminated images are more appropriate than Scheimpflug images. It appears that most of the variability arises from image capture rather than analysis. Thus, any system to be used by a sponsor should have established repeatability using a series of images captured on the same cohort of patients, rather than re-analysis of single images.

One advantage of using these systems is that the images can be stored for later analysis. An image may be compared to other images from the same patient or can be graded using a subjective grading system by a masked examiner. A further advantage is the potential for image analysis to be limited to a specified area of the capsule, e.g. the central 3 mm.

Surgical Outcomes

I stated earlier that a primary consideration should be what the patient sees. From a fiscal perspective, however, the most important outcome is whether the patient requires an additional procedure, e.g. YAG, due to the development of clinically significant PCO. Using this as the primary outcome measure in a clinical trial has the potential for clinician bias. In one of a number of papers, based on what appears to be the same data set, Hollick *et al.*¹¹ report that none of their patients receiving polyacrylic IOLs required YAG compared with 26% receiving PMMA IOLs. Nonetheless, the authors reported no significant differences in visual acuity or contrast sensitivity.

An alternative approach would be to only count the number of YAG procedures that resulted in two or more lines improvement in visual acuity, but the potential for bias still exists. For example, who decides when a patient requires YAG, and on what basis? Bias could be minimized by performing YAG on all patients after a given time interval and recording improvement in vision, but such an approach seems impractical and inappropriate.

Discussion

In summary, I propose most of the aforementioned outcome measures has some merit for randomized clinical trials of IOLs and PCO. I feel that any claims regarding degree of opacification should be based on an objective or masked subjective method that has established repeatability. The quantification of PCO should be limited to the central 3 to 5 mm and *must* be supplemented by careful visual assessment.

Finally, vision-related quality of life should be assessed using standardized instruments rather than sponsor-developed questionnaires. It is likely that instruments such as the National Eye Institute Visual Function Questionnaire (NEI-VFQ) may provide additional and important information about the benefits of certain devices based on the patients' perception of their visual function and well-being.¹²

References

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