The working relationships between the Steering Committee, the Technical Review team and the CPG panel were likewise defined to avoid bias.

This new set of guidelines is expected to reduce practice variation, discourage the use of procedures that are of minimal or questionable value, increase utilization of services that are effective but under-utilized, and target populations most likely to benefit from those services.[5] It has the potential to impact cataract management nationwide for years to come and it is our hope that this shall be regarded as a trustworthy source of recommendations where the standards of patient care and safety are ensured. Target users include but are not limited to PAO members and referring physicians, training institutions, industry partners, regulatory agencies and payors, patients and the general public.

II. GUIDELINE DEVELOPMENT METHODS

Organization of the Process

Firstly, the PAO created an administrative group, herein referred to as the Steering Committee, from the members of the PAO Committee on Standards to oversee the CPG formulation process. The Steering Committee engaged the APCEBH to provide technical support in the guideline development process.

Creation of the Evidence Base

The APCEBH Technical Review team performed an appraisal of existing guidelines on the evaluation and management of senile cataracts. Five (5) primary clinical practice guidelines from other countries[7-11] and one locally developed CPG by the PAO with Family Medicine in 2001 (with an update in 2005)[12] were appraised using validity, applicability and equity lenses. This assessment was done to determine risk of bias, generalizability and whether disadvantaged populations were considered. Arising from the individual appraisal of the six guidelines, it was recommended that the guideline development focus on the research questions prioritized by the existing guidelines; that a systematic literature search be described in detail with evidence summaries written up for each research question; that values and preferences of local stakeholders be incorporated through a multisectoral stakeholder engagement and that equity and cost issues be addressed to cover for disadvantaged populations.

Adhering to these recommendations, the Steering Committee and the Technical Review team specified the topics, drafted ten (10) priority research questions, and identified the important outcomes. The Technical Review team retrieved the relevant research articles, then appraised the directness, validity and applicability of the individual studies. They constructed evidence summaries and balance sheets for each of the 10 research questions, summarizing the trade-offs between benefit and harm. The Quality of the Evidence was assessed according to Table 2. (See also Evidence Base)

Table 2. Basis for Assessing Quality of the Evidence

Observational studies	Quality of the Evidence	Randomized trials
Extremely Strong association and no major threats to validity	High (Further research unlikely to change our confidence in estimate of effect)	No serious flaws in study quality
Strong consistent association and no plausible confounders	Moderate (Further research is likely to have an important impact)	Serious flaws in design or execution or quasi-experimental design
No serious flaws in study quality	Low (Further research is very likely to have an important impact)	Very serious flaws in design or execution
Serious flaws in design and execution	Very low (The estimate of effect is very uncertain)	Very serious flaws and at least one other serious threat to validity
Additional factors that lower quality are: • Important inconsistency of results • Some uncertainty about directness • High probability of reporting bias • Sparse data • Major uncertainty about directness can lower the quality by two levels		
Additional factors that may increase quality are: • All plausible residual confounding factors, if present, would reduce the observed effect • Evidence of a dose-response gradient		
Factors that may lead to construction of separate evidence summaries and balance sheets for disadvantaged populations: • Evidence of difference in effects in disadvantaged subgroups • Absence of direct evidence for disadvantaged subgroups		

The Technical Review team assessed the overall quality of evidence across the critical outcomes, basing this on the lowest quality of evidence for the outcomes that were critical to reaching a decision.

Balance between benefit and harm was weighed based on the critical and other important outcomes. Judgments about balance between benefits and harms did not take into account costs as shown in Table 3 (See also Appendix 1).

Table 3. Assessment of Benefits vs Harms

Category	Benefits and Harms Balance
Net Benefits	the intervention clearly doing more good than harm
Trade-offs	important trade-offs between benefits and harms
Uncertain Net Benefits	the intervention having unclear benefit over harm
No Net Benefits	the intervention clearly not doing more harm than good

Composition of the CPG Panel

Pari passu with the Technical Review team's preparation of the Evidence Base (EB), the Steering Committee undertook a systematic process of recruiting and selecting the CPG Panel considering all possible conflicts of interests of the potential panelists. To ensure fairness and transparency, this process was guided by principles and recommendations put forth by various guideline development groups.[13-17] The Steering Committee decided that the Panel would be composed of an equal number of ophthalmologists and non-ophthalmologists.

The ophthalmologists were to be chosen from nominees of the different ophthalmic groups with the understanding that they would be authorized to represent the views of their sponsoring organizations, namely: Chapter Societies of PAO, the PSCRS, the MSICS Interest Group and the PBO, and vote accordingly.

Non-ophthalmologists were either medical doctors well-versed in research methods, evidence-based medicine or CPG formulation, or, nonmedical personnel who had technical backgrounds in research, statistics, ethics, administration or policy-making. Some performed the dual role of patient advocate, having undergone cataract surgery themselves.

Formulation of the Recommendations

Recommendations were based on the trade-offs, the quality of evidence, the translation of evidence into practice in the specific situation (if specified) and uncertainty about the baseline risk. Recommendations were judged to be strong or weak based on the above, during the *en banc* Panel Review. (See Appendix 1)

For the purpose of determining the winning vote, the majority was considered to be 75% of all those who voted, i.e. 15 of 20 if all voted. Abstaining from voting was to be discouraged but not disallowed although unexpected if the evidence and the discussions were unambiguous. Two further rounds of voting on an issue would be conducted in case a majority decision was not obtained after the first round. After several rounds failing to reach a majority vote, a stalemate was to be declared and the issue would be decided again at a later date using a modified Delphi technique in order to reach a consensus. Evidence-based draft recommendations (as worded in the Evidence Base), were revised based on input arrived at by consensus in the *en banc* Panel Review.

Managing Conflicts of Interests

The Steering Committee facilitated the CPG formulation process but decided to inhibit themselves from: assessing evidence, exerting influence on research methodology and the findings of the technical team, and voting as Panelists during the *en banc* review.

Planning for Dissemination and Implementation

Ultimately, this CPG will only be useful if it becomes the reference for the standard of care for adult patients with cataract, and, if it positively influences the practice of ophthalmologists to the benefit of their patients. Wide dissemination and easy access will facilitate its utility, hence, it behooves the PAO to exert all efforts to reach all stakeholders. (See Dissemination and Implementation of the Guidelines).

The opportunity to react to the final recommendations was provided in the Public Forum with invited patient groups, healthcare providers, payors of healthcare, representatives from other specialty societies, the academe etc. Thereafter, planned implementation included a dissemination strategy, an information campaign specially targeting disadvantaged groups.

III. RESULTS

Appraisal of Existing Guidelines

The Technical Review team evaluated five (5) international[7-11] and one (1) national CPG[12]. General findings in the scan of international guidelines were that 1) there was no detailed description of the prioritization of research questions, and 2) there was no systematic searching and approach presented on how the evidence was summarized. Evidence summaries were not reported nor made available.

The National Institute for Health and Care Excellence (NICE) 2008 guidelines[9] and the PAO guidelines (2005)[12] in contrast, reported conduct of thorough literature searches and synthesis of evidence supporting the recommendations. Although the NICE 2008 guidelines[9] followed a search strategy, a number of non-English studies were removed from their yield that may have slightly affected some recommendations. The NICE 2008 guidelines[9] was also very focused on the interventional procedure (implantation of multifocal non-accommodative intraocular lenses during cataract surgery) and did not at all touch on non-surgical aspects.

A weakness common to all of the guidelines except the Royal College of Ophthalmology (RCO) 2010[10] was the lack of incorporation of values and preferences. This could have been corrected by the incorporation of informed lay groups or a representative of such lay groups in the guideline process. This was also not evident even in the local guidelines.[12]

As for the use of the GRADE approach in developing the guidelines, only the Canadian Ophthalmological Society (COS) 2008[8] was able to use the approach but it still has its limitations. None of the guidelines discussed issues on equity or targeted disadvantaged groups. In 2014, Wu and co-authors evaluated cataract surgery CPGs and arrived at similar conclusions, suggesting that stakeholder involvement must be improved to strengthen the area of values and preferences as well as applicability.[18]

The Research Questions

A total of ten (10) research questions were generated from the above guidelines scan and perceived gaps in knowledge: four (4) on comparisons of individual surgical procedures and six (6) on ancillary procedures in the management of senile cataracts. The research questions were worded as follows:

1. *Among patients with senile cataracts scheduled for surgery, will routine pre-operative testing vs. no testing reduce mortality, morbidity, and adverse events?*
2. *Among patients with senile cataracts for cataract surgery, will routine lacrimal duct irrigation reduce post-operative endophthalmitis and adverse effects?*
3. *Among patients with senile cataracts scheduled for surgery, will routine 5% povidone-iodine solution reduce post-operative endophthalmitis and adverse events?*
4. *Among patients with senile cataracts scheduled for surgery, will routine perioperative antibiotic prophylaxis reduce post-operative endophthalmitis and adverse events?*
5. *Among patients with bilateral senile cataracts about to undergo cataract surgery, how effective is same sitting or Immediate Sequential Bilateral Cataract Surgery (ISBCS) vs delayed operation or Delayed Sequential Bilateral Cataract Surgery (DSBCS) in preventing infection and reducing costs?*
6. *Among patients with senile cataracts, how effective is Manual Small Incision Cataract Surgery (MSICS) vs ECCE in improving vision and in terms of adverse outcomes/complications?*
7. *Among patients with senile cataracts, how effective is Manual Small Incision Cataract Surgery (MSICS) vs Phacoemulsification in improving vision and in terms of adverse outcomes/complications?*
8. *Among patients with senile cataracts, how effective is Phacoemulsification vs ECCE, in improving vision and in terms of adverse outcomes/complications?*
9. *Among patients with senile cataracts, how effective is Femtosecond Laser-assisted Cataract Surgery (FLACS) vs. conventional Phacoemulsification in improving vision and in terms of adverse outcomes/complications?*
10. *Among patients who develop posterior capsular opacification (PCO) after cataract surgery, how safe is less than 6 months versus 6 months and beyond Nd:YAG Laser capsulotomy in preventing macular edema, retinal damage, anterior chamber reactions and other adverse events?*

The Technical Review team then systematically searched the medical literature for the best available evidence for each of the research questions. Technical Review team members retrieved systematic reviews, randomized controlled trials and other research articles then appraised the directness, validity and applicability of each. For each of the questions and specific outcomes, evidence summaries and balance sheets were prepared. These summaries and balance sheets were then compiled, recommendations drafted and incorporated into the Evidence Base (EB) for the CPG on Management of Senile Cataracts.

The CPG Panel

A total of 20 panelists were eventually selected from more than 30 nominees by the Steering Committee using weighted criteria. Nineteen (19) of the 20 confirmed participants made it to the en banc review on June 9, 2016; the absentee was called for an emergency meeting at the Department of Health. Among those who were not eye doctors were 3 nurses, 2 economists, 2 biostatisticians, an internist/ infectious disease specialist and a family medicine practitioner. There were 12 males and 7 females. The average age of the panelists was 54 years. At least 2 had experienced cataract surgery first hand. The CPG Panel in the en banc meeting developed judgments by consensus on each intervention, weighing the relative importance of their various outcomes and discussed acceptability, appropriateness and feasibility using the nominal group technique.

Final Recommendations

For each of the questions, the Panelists deliberated on the relative importance of the outcomes. They weighed the relative importance of outcomes scoring these from 1 to 9: with outcomes scoring from 1 to 3 as not so important; from 2 to 6 as important; and from 7 to 9 as critical (See Appendix 1). The Panelists considered all the reported outcomes critical.

Ten pre-determined specific questions were tackled by the Panelists to formulate recommendations. For each question, the session moderator explained the question to clarify the premise. Afterwards, a summary of the results of literature review responding to the question was presented, particularly the critical outcomes in relation to the procedure being discussed. This was followed correspondingly by a draft recommendation from the team based on the collected evidence.

Upon discussion of the available evidence and draft recommendation, the nominal group technique was employed to generate responses where each of the panelists were instructed to give concise 3 to 4 sentence inputs. Voting commenced afterwards, and consensus arrived at by majority rule and Delphi method when required (See Guideline Development Method). At the end of the session, the resulting recommendations and votes were presented to the plenary in summary for final validation.

Judgments on all but one of the 10 draft recommendations, as modified during the discussion, passed consensus by the Panelists in the en banc session. The only question that had to proceed to a Delphi survey was "Among patients with senile cataracts, how effective is Manual Small Incision Cataract Surgery (MSICS) vs ECCE in improving vision and in terms of adverse outcomes/ complications?" (See Section Phacoemulsification vs ECCE).

IV. EVIDENCE AND RECOMMENDATIONS

1. Routine Medical Pre-operative Testing

Based on moderate level of evidence, there was no significant difference in the rates of intraoperative or post-operative ocular and medical adverse events between routine medical pre-operative testing and no routine medical pre-operative testing.

A meta-analysis of 3 randomized controlled trials that included 21,531 cataract surgeries done under local anesthesia showed that overall risk for adverse medical events from cataract surgery was low (3 out of 100 surgeries)[19]. The rate of adverse events was similar between the routine pre-operative testing group (353 events out of 10,764 surgeries) and the no routine testing group (354 events out of 10,766 surgeries). Adverse events were mostly cardiovascular in nature (e.g. half were blood pressure elevations requiring treatment) and occurred intra-operatively. The rate of postponement or cancellation of surgery was also similar in the 2 groups (161 out of 10,287 surgeries in the routine testing group vs. 166 out of 10,295 surgeries in the no testing group)[20,21] Cost was evaluated in one study, which estimated that the cost was 2.5 times higher in those who underwent pre-operative testing than those who did not.[20]

Only one study reported rates of myocardial infarction, stroke, and hypoglycemia within 7 days of cataract surgery separately[21]. There was no difference between routine testing and no testing for these outcomes, however confidence intervals for the results were wide, because event rates were very low (less than 10 in 10,000 in both groups). None of these events occurred intra-operatively.

Majority of the participants enrolled in the included studies were patients with mild to severe, non-incapacitating systemic diseases (e.g. hypertension, diabetes, congestive heart failure, and bleeding disorders). Routine pre-operative tests included ECG, CBC, blood sugar, serum electrolytes, BUN and creatinine. Outcomes evaluated were ocular complications, medical adverse events requiring treatment, and postponement or cancellation of surgery.

The results of the meta-analysis were driven mainly by the largest study in the meta-analysis, which included a total of more than 19,000 surgeries[21]. However, this trial was methodologically sound, and the results were consistent across all the studies included in the meta-analysis.

Given these findings, routine medical pre-operative testing is not recommended for patients with senile cataracts scheduled for surgery.

Recommendation 1

Pre-operative medical ancillary testing prior to cataract surgery is recommended only if indicated by the patient's medical condition and the physician's assessment.

(Strong recommendation. Moderate to high quality evidence.)

Remarks

The physician must still determine a patient's health status through history taking and physical examination. It was emphasized that "pre-operative testing" referred to the local procedure of "clearance" with ancillary testing totally separate from the routine history-taking and physical examination.

2. Routine Lacrimal Duct Irrigation

There is no randomized trial found in the literature search to answer the research question. Instead, a prospective cohort study is available where 282 (40%) patients who received no lacrimal system irrigation nor topical antibiotic prior to surgery was compared to 418 (60%) patients who received lacrimal system irrigation with or without neomycin eye drops[22]. No patient developed post-operative endophthalmitis in both groups. Although the overall bacterial contamination was reported at 14.1%, the actual number of patients per group was not mentioned. (See Appendix 3: EB Table 2).

Recommendation 2

Lacrimal duct irrigation as a routine pre-operative procedure in cataract surgery does not reduce the incidence of endophthalmitis but may be performed when indicated.

(Strong Recommendation. Very low quality evidence.)

Remarks

With very low quality evidence, the panel decided NOT to recommend routine lacrimal duct irrigation because of low incidence of post-operative infections and even the risk of contamination with the procedure. In lieu of lacrimal duct irrigation, massaging the lacrimal sac to elicit purulent discharge from the puncta may be a better, less invasive way of determining if active dacryocystitis is present and prior treatment is indicated. Patients complaining of tearing and discharge or other symptoms of dacryocystitis, and, a prior history of lacrimal duct surgery are good indications to perform the procedure.

3. Routine Povidone-Iodine Solution

There is one randomized controlled trial (RCT) and one prospective cohort study found in the literature search to answer the research question. The RCT however does not specify the concentration of Povidone-Iodine (PI) solution used[23]. A total of 4111 eyes underwent cataract surgery and were included in this study. There was no significant difference between the PI group and the control (silver protein)

group (RR 1.17, 95% CI 0.57 – 2.42). The prospective cohort study including 8,083 eyes showed significant difference between 5% PI and no 5% PI (p <0.03)[24]. However, on rechecking, it turned out that this is not significant (RR 0.24, 95% CI 0.57 – 1.08). Pooled analysis of these two studies (PI vs control) showed a trend of benefit toward PI with an RR of 0.61 (95% CI 0.13 – 2.86, I2 72%). These two studies are both low quality.

In several case reports, conjunctival irritation is seen in 0.4%[25]. Contact dermatitis is less common (0.04%); however, the risk increases tenfold in the presence of allergy to shellfish or iodine[26]. Despite the increased risk for allergy, patients are still recommended to receive PI prior to surgery.[27] Keratoconjunctivitis sicca has also been reported[27]. Hyperemia of conjunctivae, superficial punctate epitheliopathy and epithelial defect, corneal symptoms (edema or Descemet's membrane folds), and mild to moderate Tyndall were seen in randomized trial comparing different concentrations of PI solutions[26].

Recommendation 3

Instillation or irrigation of the conjunctiva with 5% povidone iodine solution pre-operatively is recommended to reduce the risk of post-operative endophthalmitis.

(Strong Recommendation. Very low to low quality evidence.)

Remarks

Despite the low to very low quality of evidence in published literature on its effectivity in reducing the incidence of endophthalmitis and because of the relatively low incidence of adverse events in its use, the instillation of 5% povidone-iodine solution was considered to be a prudent measure in ensuring asepsis of the ocular surface during surgery.

4. Routine Peri-operative Antibiotic Prophylaxis

There were three (3) randomized controlled trials found in the literature search to answer the research question but investigated different kinds of antibiotics. One RCT compared topical regimen (chloramphenicol-sulphadimidine ointment) plus periocular penicillin at the time of surgery with topical regimen alone[28]. This study done in northern Pakistan found significant reduction of endophthalmitis with topical regimen plus periocular penicillin (RR 0.33, 95% CI 0.12–0.92) during surgery compared with topical regimen alone. In another RCT conducted in Turkey, balanced salt solution (BSS) irrigation with vancomycin and gentamycin was compared to BSS alone showed no benefit from vancomycin and gentamycin (RR 0.20, 95% CI 0.01–4.15)[29]. The last RCT of high quality evidence was based on a 2 x 2 factorial design, with intracameral cefuroxime and topical perioperative levofloxacin resulting in 4 treatment groups[30]. This was conducted by the European Society of Cataract & Refractive Surgeons (ESCRS) involving 16,603 eyes of 16,603 patients from multiple sites in Europe and Turkey. The results of this study showed that intracameral cefuroxime alone (RR 0.20, 95% CI 0.04–0.91) and combined intracameral cefuroxime with topical levofloxacin (RR 0.10, 95% CI 0.27–0.78) showed significant reduction in endophthalmitis as compared to no antibiotic prophylaxis. However, the reduction of endophthalmitis with topical levofloxacin alone as compared to no antibiotics was not statistically significant (RR 0.70, 95% CI 0.27–1.84). Other comparisons such as intracameral cefuroxime vs topical levofloxacin, combined intracameral cefuroxime and topical levofloxacin vs intracameral cefuroxime, intracameral cefuroxime and topical levofloxacin vs topical levofloxacin did not result in significant reduction in endophthalmitis. There was also no statistically significant reduction in the final visual acuity following endophthalmitis among patients given intracameral cefuroxime with/without topical levofloxacin as compared to no intracameral cefuroxime with/without topical levofloxacin.

Despite this reduction in endophthalmitis, a number of case reports and case series have been published on harm of intracameral and intravitreal cefuroxime. Anterior and posterior segment inflammation were reported in six patients with high doses of intracameral cefuroxime.[31] All six patients in this series had satisfactory final visual outcome even without surgical intervention. Inadvertent overdose of cefuroxime caused hemorrhagic retinal infarction in four patients[32] and macular infarction and associated cystoids macular edema.[33] Two patients developed anaphylactic reactions from intracameral[34] and intravitreal[35] cefuroxime.

Recommendation 4

The use of peri-operative antibiotic prophylaxis is recommended to reduce the risk of post-

operative endophthalmitis in patients who undergo cataract surgery.

(Strong recommendation. Moderate quality evidence.)

Remarks

Since most of the antibiotics in the studies are not used locally, the panel could not recommend specific antibiotics nor protocols for the peri-operative prophylaxis.

5. Immediate versus Sequential Bilateral Cataract surgery

Based on a low-quality cohort study, the risk of infection in delayed sequential bilateral cataract surgery (DSBCS) with intracameral prophylactic antibiotics is very small (1 in 29,582). A nonsignificant 2-fold increase in the risk of infection was observed among immediate sequential bilateral cataract surgery (ISBCS) patients who were given prophylactic intracameral antibiotics[36].

The subjective improvement in visual function is not significantly different in ISCBS and DSCBS patients based on a meta-analysis[37] of 2 randomized studies[38,39]. The two trials had conflicting results for this outcome and were significantly dissimilar. There is also no statistically significant difference in the risk of any intra- and post-operative complications (capsule tears, vitreous loss, iridectomy, sphincterotomy, sutures in wound, intraocular pressure >30 mmHg, wound leak IOL decentration or deplacement, anterior chamber flare, capsular fibrosis, capsule opacification, foreign body sensation, dry eyes and more serious complications such as corneal edema, macular edema, wound leak, or iris prolapse) between patients who underwent ISCBS and DSCBS[38,39]. Likewise, there is no statistically significant difference in the risk of serious post-operative complications (corneal edema, macular edema, wound leak, or iris prolapse) between the aforementioned groups.[38,39].

Canadian estimates of crude cost savings from ISCBS over DSCBS is pegged at US$ 1,606 (valued in 2013) per patient with adjusted estimates pegged at US$ 1,431 per quality-adjusted life-year (QALY)[40] gained. Converting these based on the 2013 average peso-dollar exchange rate, crude cost savings amount to Php 68,202 per patient while adjusted cost savings is Php 60,746 per QALY gained. Considering the number of patients needing cataract surgery, the cost savings can be substantial even if we consider cost variation in different countries. In the Philippines, it is also important to consider the opportunity cost for the caregiver or watcher (*bantay*) of the patient. Often, patients will come for consultations and procedures with a handful of *bantays*. The collective loss of productivity and earnings of these *bantays* are substantial and may confer additional cost savings in favor of ISCBS.

Aside from benefits in terms of costs, ISCBS confers additional benefits to patients: rapid visual recovery and functional advantage in the short term. ISCBS patients tend to regain visual functions earlier than their DSCBS counterparts. Unfortunately, among patients who underwent ISCBS, the very short interval between the surgeries of the two eyes precludes adjustments in surgical plans based on the result of the first eye surgery[41].

Recommendation 5

Delayed Sequential Bilateral Cataract Surgery is preferred over Immediate Sequential Bilateral Cataract Surgery (ISBCS) in the same sitting for patients with bilateral senile cataracts.

(Strong recommendation. Very low to low quality evidence.)

Remarks

The possibility of bilateral endophthalmitis, no matter how small its probability, and the devastating effect on the patient should such occur, outweighed the potential cost benefit of same sitting surgery which came from very low to low quality evidence anyway.

6. MSICS versus ECCE for senile cataracts

Evidence from 2 randomized controlled trials showed that there was no significant difference in terms of improvement of visual acuity at 6-8 weeks between MSICS and ECCE with a relative risk (RR) of 1.57 (95% CI 0.88, 2.8)[42,43]. However, the data presented in these 2 RCTs reporting poor visual outcome were not combined due to difference on how the measurements were made. Both RCTs reported an insignificant difference between the 2 procedures with regards poor visual outcomes at 6-8 weeks. One study reported an RR of 1.58 (95% CI 0.45, 5.0) supporting the insignificance of the findings.[42]

Surgically-induced astigmatism was significantly less for MSICS. One study reported a mean induced astigmatism in diopters of 1.77 ± 1.65 for ECCE vs 1.1 ± 0.95 for MSICS, p=0.012.[43] In another study, the incidence of astigmatism of ≥2D had a relative risk of 0.49, (95% CI 0.32-0.74) indicating less astigmatism in the MSICS technique.[43]

Intraoperative and post-operative complications based on 1 RCT, were significantly higher with MSICS, with relative risks of 1.83 (95% CI 1.02-3.26), and 1.38 (95% CI 1.1-1.73), respectively.[42] Both intraoperative and post-operative complications reported in the RCT were graded and scored as described by the Oxford Cataract Treatment and Evaluation Team (OCTET).

There was a limited number of studies with issues on allocation and concealment. It was unfortunate that most of the data could not be combined due to differences in reporting of outcomes.

Recommendation 6

MSICS is the preferred technique for cataract surgery over ECCE because of less surgically induced astigmatism.
(Strong recommendation.
Low to moderate quality evidence.)

Remarks

Complicated MSICS surgeries usually performed by novice surgeons not properly acquainted with the technique has led many surgeons to prefer ECCE. This initial negative bias and higher risk of complications in MSICS would be mitigated by improving access to training and thereby the surgical expertise in MSICS.

7. MSICS versus phacoemulsification in senile cataracts

Evidence for MSICS versus phacoemulsification for the outcome of good functional vision at 3 months (uncorrected acuity 6/18 or better from 6-8 weeks of follow-up) showed significant benefit in favor of phacoemulsification with a relative risk (RR) of 0.90 (95% CI 0.84, 0.96) based on 3 randomized controlled trials.[45-47]

Other evidence summarized and combined from 13 RCTs[45-47] and 3 meta-analyses[58-60] failed to show significant difference in the following:

1. Good functional vision at 6 months (uncorrected acuity 6/18 or better) based on 1 RCT, with an RR of 1.07 (95% CI 0.91, 1.26).[54]
2. Good functional vision at 3 months (best-corrected acuity 6/18 to 6/12 or better) based on 6 RCTs, with an RR of 0.99 (95% CI 0.98, 1.01).[45-47, 59-61]
3. Good functional vision at 6 months (best-corrected acuity) based on 1 RCT, with an RR of 1.0 (95% CI 0.94, 1.06).[54]
4. Poor visual outcome at 3 months (best corrected acuity worse than 6/60), OR 2.48 (95% CI 0.74, 8.28).[45-47, 49-51]
5. Poor visual outcome at 6 months (best-corrected acuity worse than 6/18) based on 1 RCT is 1.9% in both groups with a computed RR of 1.0 (95% CI 0.06, 16).[54]
6. Uncorrected visual acuity in 1 week after surgery, RR 1.0 (95% CI 0.97, 1.03).[46,48,53,56,57]

Furthermore, neither surgical technique showed clear benefit in preventing any of the complications such as posterior capsular rupture,[45-47, 49-58] corneal edema postoperatively,[45-47, 50-53, 55-58] endothelial cell loss[49,51], and astigmatism.[46,47,49,51,56]

In light of the evidence, it seems that phacoemulsification has an edge over MSICS in terms of visual acuity improvement. Although astigmatism may be an issue, it has not been clearly established with the current evidence.

Recommendation 7

Phacoemulsification is the preferred technique for cataract surgery over MSICS because of faster visual improvement and lower risk of adverse events or complications.
(Strong recommendation.
Very low to low quality evidence.)

Remarks

The cost of the equipment and surgical consumables in phacoemulsification raises the issue of equity and accessibility for disadvantaged groups. Hence, in areas where phacoemulsification is not available or feasible, surgical expertise in MSICS must be developed as an alternative. Although faster visual rehabilitation, due to less surgical trauma in phaco-

emulsification, is a patient-valued outcome, over time MSICS and phacoemulsification achieve similar results.

8. Phacoemulsification versus ECCE for senile cataracts

These findings were derived from 6 randomized controlled trials (RCT)[61-66] and 1 meta-analysis[57]. In the combined analysis, it was noted that good functional vision at 3 months (uncorrected visual acuity and best corrected visual acuity) significantly favored phacoemulsification.[61-64] Good functional vision at 12 months, in terms of uncorrected visual acuity, also significantly favored phacoemulsification.[62] However, at 12 months, measured by best corrected visual acuity, the difference between phacoemulsification and ECCE was insignificant.[62]

Poor visual outcome at 3 months, in terms of best corrected acuity of 6/60 or worse, was significantly lower in phacoemulsification.[61-61] However, after 12 months, this outcome was insignificant between phacoemulsification and ECCE.[62]

Adverse events or complications that did not show any significant difference between the 2 techniques were capsular rupture[62,63,65], retinal detachment[62] and endothelial cell loss[62,62,66]. However, posterior capsular opacification[62,65], cystoid macular edema[62,65] and iris prolapse[62] are complications that were significantly lower with phacoemulsification.

The studies generally had an unclear risk of bias due to poorly reported trial methods and although the quality per outcome ranged from low to moderate, overall quality of evidence was deemed low for this recommendation.

Recommendation 8

Phacoemulsification is the preferred technique for cataract surgery over ECCE because of significant benefits and lower risk of complications.

(Strong recommendation. Low to moderate quality of evidence.)

Remarks

The benefits derived from the smaller incision, including faster visual rehabilitation and less risk of devastating complications associated with larger incisions, make phacoemulsification favorable over ECCE.

9. Femtosecond laser-assisted cataract surgery (FLACS) versus conventional phacoemulsification in senile cataracts

There was no significant difference between FLACS and conventional phacoemulsification in the overall result, in terms of improvement in vision, measured by uncorrected distance visual acuity.[68,69] The difference was also insignificant when subgrouped by follow-up time (at 1 week, 1 month and 6 months).

As for improvement in vision (measured by corrected distance visual acuity), there was a significant difference favoring FLACS when looking at the overall result, with a mean difference of -0.03 LogMAR units. This implies a significant improvement of visual acuity by 0.03 using the LogMAR chart favoring FLACS. The difference is also significant at 1 week and at 6 months postoperatively.[69-73]

However, among the adverse outcomes, the differences were insignificant between FLACS and conventional phacoemulsification in the rates of anterior capsule tear[71,72], elevated intraocular pressure[71,73], and macular edema[71,72].

One study showed that based on the *simulated* complication rates of phacoemulsification and FLACS and assuming resultant visual acuity outcome improvement of 5% in uncomplicated cases of FLACS, the cost-effectiveness (dollars spent per QALY) gained from FLACS was not cost-effective at AUD $92,862.[74]

There were 7 RCTs [68-74] and 1 meta-analysis[69] that showed these findings. Unfortunately, there was unclear to high risk for bias for the included studies. These were mainly from issues with randomization and allocation concealment. The studies were also at high risk for performance and detection bias. Consistency issues were seen in the primary outcomes, but not evident in the complications.

Recommendation 9

The choice of FLACS or conventional phacoemulsification for routine cataract surgery will

depend on accessibility, surgeon experience, and patient cost preferences.
(Weak recommendation. Very low evidence.)

Remarks

FLACS has not shown superior visual acuity results over conventional phacoemulsification and, in the light of cost concerns and limited access to the technology, FLACS was not recommended over phacoemulsification.

10. Nd:YAG Laser Capsulotomy

Three studies were identified addressing the adverse effects of Nd:YAG laser capsulotomy in patients with PCO but none of these studies compared the less than 6 months versus 6 months and beyond in timing of the capsulotomy. One study however compared different time durations from 6 months up to greater or equal to 37 months[75]. The sample sizes were 23[76], 31[77] and 314[75] adult patients, with follow-up observations ranging from as early as immediately after the procedure to three months post-capsulotomy.

From the very low quality evidence from the two studies with small sample sizes, the limited available data does not seem to show any statistically significant difference ($p < 0.05$) between the anterior chamber depth, intraocular pressure, macular foveal thickness and endothelial cell loss before and after the capsulotomy[76,77].

However, the cohort study by Shaikh et al.[75] in 2010 demonstrates that laser capsulotomy may induce potential complications, e.g. anterior chamber reactions, intraocular pressure, damage to intraocular lenses, retinal detachment, macular edema and vitreous hemorrhage.

Recommendation 10

Regardless of time elapsed after cataract surgery, Nd:YAG Laser Capsulotomy is only recommended in patients who develop symptomatic posterior capsular opacification, because of the risk of macular edema, anterior chamber reaction, retinal detachment and other adverse events which may be associated with the procedure.
(Strong Recommendation. Very low quality evidence.)

Remarks

There is no evidence that the timing of laser capsulotomy influences the probability of the occurrence of potential complications suggesting that other criteria should be used to determine appropriateness of treatment.

V. RESEARCH IMPLICATIONS

The Technical Review team, the CPG Panel and the Steering Committee identified important knowledge gaps that need to be addressed through primary research.

These gaps were especially evident in the research questions for which evidence was deemed very low to low quality: Routine lacrimal duct irrigation; Routine 5% povidone-iodine solution; Immediate versus sequential bilateral cataract surgery; Phacoemulsification vs MSICS; (FLACS) versus conventional phacoemulsification; Nd:YAG Laser capsulotomy.

Important research gaps were also pinpointed even for the research questions for which the evidence was deemed of moderate quality. Particular note is made of the lack of local data on the comparative effectiveness and safety of MSICS vs ECCE and MSICS vs phacoemulsification. This paucity of data has important equity issues, given the limited number of experts in MSICS and the resultant inaccessibility particularly of disadvantaged groups to this procedure.

It must be noted that the evidence base for the various cataract surgery procedures consisted of comparisons between individual procedures. Panelists *en banc* were able to formulate a "ranking" as an interim summary as follows: Phacoemulsification recommended over MSICS; Phacoemulsification recommended over ECCE; Neutral on phacoemulsification versus FLACS, and; undecided on MSICS versus ECCE (the latter was resolved after 2 rounds of Delphi surveys, concluding with MSICS recommended over ECCE). It was emphasized though that strictly seeking, such a "ranking" should be based on the results of a "network meta-analysis", this being a priority research gap that merits attention.

Other gaps included: local cost-effectiveness data, e.g. expressed in QALYs; data on specific

outcomes of visual improvement, e.g. immediate return to function as might be a more relevant outcome for disadvantaged groups like farmers and drivers, astigmatism as an outcome in the comparisons between phacoemulsification and MSICS, etc.; comparative safety between phacoemulsification and ECCE (arising from poorly reported trial methods and thus an unclear risk of bias in existing published reports); data on efficacy and safety of locally used antibiotics for routine perioperative antibiotic prophylaxis; publication of data on efficacy and safety of the commonly used 5% povidone-iodine for antisepsis.

Another important gap that was evident in the discussions, was that of a "mapping" of practitioners with expertise and facilities capacitated for particular cataract surgery procedures, e.g. for MSICS and phacoemulsification, the latter especially as it is a more costly procedure requiring special equipment. This has important implications to equity and targeting of disadvantaged groups.

A policy gap that needs to be addressed especially because of its implications to health financing was that of strengthening standardization of the practice of Nd:YAG Laser Capsulotomy for symptomatic posterior capsular opacification.

VI. DISSEMINATION AND IMPLEMENTATION

Dissemination to the PAO Members

The CPG was presented during the 2016 PAO Annual Convention. Copies had been mailed to the members two weeks ahead of the meeting for their perusal. Comments and questions were elicited during the discussion period for the purpose of clarifying the recommendations. A full copy of the document is published on-line in the PAO website aside from this Philippine Journal of Ophthalmology (PJO) supplement.

Dissemination to the Training Institutions

The Philippine Board of Ophthalmology (PBO) was asked to endorse the CPG. Copies of the CPG with the PBO endorsement will be sent to the heads of hospital-based departments of ophthalmology, training institutions and ambulatory surgery centers, the Philippine Board of Medicine of the Professional Regulatory Commission, the Association of Philippine Medical Colleges Foundation, Inc., medical schools and libraries so as to incorporate the recommendations in their teaching and training curricula, with the support of the consultants and mentors.

Dissemination to Industry Partners, Regulatory Agencies, and Payors

The CPG will be transmitted to pharmaceutical industry partners; NGOs involved in eye care; health maintenance organizations (HMOs); the Department of Health and the Philippine Health Insurance Corporation through formal communications by the PAO Council.

Dissemination to the Patients and the Public in General

A simplified version of the CPG shall be formatted and made available to the PAO members in a format that will be ready for reproduction and dissemination to their patients in their clinics. The same will be available for interested parties who might browse the PAO website.

Implementation and Monitoring

A questionnaire will be distributed annually for the purpose of determining the preferred practices of PAO members with regard to cataract surgery. The results shall be compiled and tracked annually to monitor convergence of practice patterns with the CPG recommendations.

VII. APPLICABILITY ISSUES

The PAO guideline development group using equity and applicability lenses flagged some caveats here re-emphasized:

The recommendation to not do routine pre-operative ancillary testing on healthy adults with cataracts are separate from the history taking and physical examination that are essential in their pre-operative evaluation. Should the history taking and physical examination uncover high risk conditions, this subgroup of patients may require direct testing under the individual discretion of their clinicians.

Though the cost of phacoemulsification is prohibitive (largely because of the need for expensive equipment), it is the preferred procedure over ECCE and MSICS from the weighed tradeoff between benefits and harm.

Though the surgical expertise in MSICS may not yet be widely distributed an increase in the capacity and improvement in accessibility to this procedure is being discussed, with more ophthalmologists trained in this procedure and deployed or committed to conduct periodic visits to disadvantaged groups in remote areas.

VIII. UPDATING OF THE GUIDELINES

PAO plans to review these practice guidelines by 2018. The recommendations in the CPG shall hold until such time that technology, patient and provider preferences, or new evidence provides the impetus for revisiting and updating the guideline once more.

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