POEMs

Repeat Cytology Within Six Months Equals Colposcopy for Younger Women with ASCUS or LSIL

Clinical Question

Is colposcopy with biopsy better than repeat cytology alone within six months to prevent invasive cervical neoplasia?

Bottom Line

Among women 22 to 27 years of age with an index cervical cytology showing abnormal squamous cells of undetermined significance (ASCUS) or low-grade squamous intraepithelial lesion (LSIL), the incidence of invasive cervical cancer did not differ between repeat cytology within six months or colposcopy with biopsy within six months. For women 28 years or older, there was an increased risk of invasive disease with the repeat cytology approach. Among the younger women, there was an increased incidence of invasive disease using an interval for cytology of seven to 12 months. An initial follow-up approach for the younger group using cytology only within six months would avoid 27% of colposcopic procedures in that group and save significant health care resources. Note that colposcopies that did not include any histologic specimen were classified as cytology only. (Level of Evidence = 2b)

Synopsis

This large cohort study from Sweden includes all women in the country 22 to 50 years of age who underwent cervical cancer screening between 1989 and 2011 (N = 2,466,671). Multiple national registries were linked and are believed to be complete. Women were followed from their first registered cytology until diagnosis of invasive cancer, total hysterectomy, emigration, death, or the end of 2011, whichever came first. Median follow-up was 9.9 years. Cervical cancers diagnosed within six months of the initial cytology were considered prevalent cancers. Cancers diagnosed between 0.5 and 6.5 years after the index cytology were considered incident cancers. The authors identified women with an index cytology showing ASCUS or LSIL and analyzed the follow-up. Follow-up was classified as cervical histology, cytology only (which included any colposcopy without biopsy), or no morphologic follow-up. Analysis of crude incidence by age showed differing risks for women 22 to 27 years of age (n = 71,449) vs. women 28 to 50 years of age (n = 119,528). Incident cervical cancer for the younger group did not differ whether initial follow-up was histologic or repeat cytology within six months (incidence rate ratio = 2.0; 95% confidence interval, 0.6 to 6.5), but was higher if cytology was performed at seven to 12 months (incidence rate ratio = 5.3; 95% confidence interval, 1.1 to 20.0). For older women, the risk of incident cancer after ASCUS or LSIL was much higher and the incident rate ratio within six months was apparently statistically significant, but it was not reported in the paper.

Study design: Cohort (retrospective)

Funding source: Government

Setting: Population-based

Reference: *Sundström K, Lu D, Elfström KM, et al. Follow-up of women with cervical cytological abnormalities showing atypical squamous cells of undetermined significance or low-grade squamous intraepithelial lesion: a nationwide cohort study.* Am J Obstet Gynecol. *2017;216(1):48.e1-48.e15.*

LINDA SPEER, MD

Professor and Chair, Department of Family Medicine
University of Toledo, Toledo, Ohio

PCI Has More Benefits and Harms Than CABG for Selected Patients with Left Main Coronary Artery Disease

Clinical Question

For selected patients with left main coronary artery disease, is percutaneous coronary intervention (PCI) with a drug-eluting stent an option to replace coronary artery bypass grafting (CABG)?

Bottom Line

The authors of this study—which was sponsored by a manufacturer of stents—argue that the results prove that PCI is just as good as CABG for many patients with a left main lesion. A deeper dive into the data suggests that it is not quite so clear. Patients undergoing PCI had fewer early myocardial infarctions, but more later deaths and later myocardial infarctions. There are other benefits to PCI, including shorter hospital stay, lower cost, and faster recovery. But patients should be informed of the trade-offs, and it is important to look at longer-term outcomes beyond three years (which the investigators promise to do). (Level of Evidence = 1b)

Synopsis

Guidelines in Europe and the United States continue to recommend CABG as the preferred treatment for all patients with left main coronary artery disease. However, subgroup analyses in previous trials suggest that some patients may do just as well with a drug-eluting stent. This study included 1,905 patients with left main coronary artery disease (defined as at least 70% stenosis, or 50% to 70% stenosis judged to be hemodynamically significant) and low to intermediate anatomic complexity (SYNTAX score < 32). The patients were randomized to receive CABG or PCI with a drug-eluting stent. The average age of participants was 66 years, 77% were men, 91% were white, 56% lived in Europe, and 39% lived in the United States. Approximately 29% had diabetes mellitus, 15% had experienced a recent myocardial infarction, 17% had a previous PCI, and 16% had renal insufficiency. The primary end point was a composite of death, stroke, or myocardial infarction at three years. Groups were similar at the start of the study, and analysis was by intention to treat. This study was designed as a noninferiority trial, defining "just as good" as no more than 4.2% worse in terms of the primary composite outcome.

Most patients (935 out of 948 in the PCI group and 923 out of 957 in the CABG group) received their assigned treatment. At three years, there was no significant difference between groups in the composite outcome (15.4% for PCI vs. 14.7% for CABG; $P = .98$), and this met the criteria for noninferiority. Not surprisingly, the primary outcome was less common in the first 30 days in the PCI group, driven primarily by fewer strokes and myocardial infarctions (4.9% vs. 7.9%; $P = .008$; number needed to treat to harm [NNTH] = 30). However, buried in Appendix Table S9 was the fact that the primary end point was more common in the PCI group between 30 days and three years, driven primarily by more deaths and more myocardial infarctions (11.5% vs. 7.9%; $P = .02$; NNTH = 28). All-cause mortality was higher in the PCI group (8.3% vs. 6.0%), although statistical significance is not reported. The need for subsequent revascularization because of ischemia was also higher in the PCI group (12.6% vs. 7.5%; $P < .001$; NNTH = 20). The study was open label, which may have affected subsequent treatment decisions, including the need to revascularize.

Study design: Randomized controlled trial (nonblinded)

Funding source: Industry

Allocation: Concealed

Setting: Outpatient (specialty)

Reference: *Stone GW, Sabik JF, Serruys PW, et al.; EXCEL Trial Investigators. Everolimus-eluting stents or bypass surgery for left main coronary artery disease.* N Engl J Med. *2016;375(23):2223-2235.*

MARK H. EBELL, MD, MS
Professor
University of Georgia, Athens, Ga.

Placebo Plus Message of Benefit Decreases Chronic Low Back Pain

Clinical Question

Can simply telling patients that a medicine works, even if it is placebo, decrease pain and improve disability in patients with chronic low back pain?

Bottom Line

These investigators gave twice daily placebo to patients with chronic back pain and told them it was placebo. They also told them that placebos can have a pronounced effect (which is true). The addition of placebo to usual care improved patients' pain and disability scores over the three weeks of the study. Although we probably will not start prescribing placebo, this study emphasizes the great value of conveying one's confidence in the treatment to bolster its effect. (Level of Evidence = 2b)

Synopsis

These investigators, who conducted the study in Portugal, enrolled 83 patients who had experienced low back pain for at least three months and responded to an advertisement. Most (87%) were taking analgesia, approximately 40% were taking adjuvant medication (e.g., gabapentin [Neurontin] or a muscle relaxant), and approximately 20% were taking an antidepressant. The authors excluded patients with severe fibromyalgia or rheumatoid arthritis and those who had received opioid treatment in the past. For three weeks, patients were asked to continue their usual treatment. Using concealed allocation, one-half of the patients were also given two placebo tablets twice a day. They were told that it was an inactive placebo, but: (1) it could still have a powerful effect; (2) the body can

automatically respond to placebo; (3) a positive attitude is helpful but not necessary; and (4) the placebo must be taken faithfully. Knowingly taking placebo significantly decreased maximum reported pain, minimum reported pain, and usual pain compared with usual therapy only. Back pain–related disability was also decreased with placebo. There were several problems with the study, however: unbalanced baseline pain, small numbers in each group, and the lack of a commercially available placebo.

Study design: Randomized controlled trial (nonblinded)

Funding source: Government

Allocation: Concealed

Setting: Outpatient (any)

Reference: *Carvalho C, Caetano JM, Cunha L, Rebouta P, Kaptchuk TJ, Kirsch I. Open-label placebo treatment in chronic low back pain: a randomized controlled trial.* Pain. *2016;157(12):2766-2772.*

ALLEN F. SHAUGHNESSY, PharmD, MMedEd
Professor of Family Medicine
Tufts University, Boston, Mass.

If You Give Amoxicillin/Clavulanate to Six- to 23-Month-Olds with AOM, 10 Days Is Preferable to Five Days

Clinical Question

Is five days of amoxicillin/clavulanate (Augmentin) noninferior to 10 days of amoxicillin/clavulanate in children with acute otitis media (AOM)?

Bottom Line

These authors begin with the assumption that we should treat children who have AOM with amoxicillin/clavulanate. They demonstrated that outcomes were slightly better with 10 days of treatment compared with five days of treatment in this group of six- to 23-month-olds with rigorously confirmed AOM. The greatest benefit was in children one to two years of age who had more severe pain and fever. In children with less severe symptoms, observation should still be the preferred option, as recommended by the American Academy of Family Physicians guidelines, accompanied by appropriate treatment of pain and fever. (Level of Evidence = 1b)

Synopsis

A previous study by the same lead author (*N Engl J Med.* 2011;364(2):105-115) found some support for antibiotics in children younger than two years with AOM for the outcome of sustained resolution of symptoms at 14 days (67% vs. 53%; $P = .04$; number needed to treat [NNT] = 7), but it found no significant difference at two days, four days, or seven days. Children who received amoxicillin/clavulanate had more diarrhea (number needed to treat to harm [NNTH] = 10) and diaper dermatitis (NNTH = 6). Although that seems like a draw, at best, the authors concluded that amoxicillin/clavulanate is appropriate for treatment of AOM.

In this study, the authors identified 520 children, six to 23 months of age, with AOM based on the presence of less than 48 hours of symptoms, a score of 3 or more on a 14-point AOM symptom score, the presence of middle ear effusion, and bulging of the tympanic membrane. A total of 515 were randomly assigned to receive 10 days of amoxicillin/clavulanate or five days of amoxicillin/clavulanate followed by five days of placebo. The dose was 90-mg amoxicillin and 6.4-mg clavulanate per kg. Approximately one-half of the children were six to 11 months of age; the remainder were 12 to 23 months of age; 54% were male; and one-half had bilateral AOM. Groups were balanced at the beginning of the study, and analysis was by intention to treat. Children were evaluated at four to six days and again at 12 to 14 days. A treatment failure was defined as worsening symptoms, worsening tympanic membrane bulging, or lack of complete or nearly complete symptom resolution. Children who experienced a clinical failure received rescue therapy with additional broad-spectrum antibiotics.

At the end of treatment, the likelihood of clinical failure was greater in the five-day group than in the 10-day group (34% vs. 16%; 95% confidence interval for difference, 9% to 25%; NNT = 6). The magnitude of this difference between groups was greater for children 12 to 23 months of age than for younger children (24% vs. 11%) and for children with more severe pain and fever on presentation (27% vs. 6%). The likelihood of a greater than 50% reduction in the symptom score from baseline was higher in the 10-day group, although not by much (91% vs. 80%; $P = .003$; NNT = 9). There was no difference in the likelihood of diarrhea or diaper dermatitis between groups: five days were as bad as 10 days, with approximately one-third of the children experiencing each of these adverse effects.

Study design: Randomized controlled trial (double-blinded)

Funding source: Government

Allocation: Concealed

Setting: Outpatient (primary care)

Reference: *Hoberman A, Paradise JL, Rockette HE, et al. Shortened antimicrobial treatment for acute otitis media in young children.* N Engl J Med. *2016;375(25):2446-2456.*

MARK H. EBELL, MD, MS
Professor
University of Georgia, Athens, Ga. ■