

POEMs

Patient-Oriented Evidence That Matters

Incidental Findings Are Common with Chest CT and MRI of the Spine and Brain

Clinical Question

What is the likelihood and what are the outcomes of incidental findings on imaging tests?

Bottom Line

The risks of imaging, in addition to radiation exposure, include the identification of incidentalomas, which can lead to patient anxiety, further testing, and overtreatment. There is little research to guide what to do when they pop up on an imaging report (as the famous dodge “clinical correlation needed”). Computed tomography (CT) of the chest (45%), CT colonoscopy (38%), and cardiac magnetic resonance imaging (MRI) (34%) commonly produce incidental findings. The rate of malignancy in incidentalomas was high in breast (42%) and ovary (28%) findings; intermediate in prostatic and colonic (10% to 20%) findings; and low in brain, parotid, and adrenal gland (less than 5%) findings. Although everyone has a story of the lifesaving results of such serendipity, we do not often consider the patients subjected to unneeded testing and treatment, the so-called victims of modern imaging technology—you can figure out the acronym (*BMJ*. 2003;326:1273). (Level of Evidence = 2a)

Synopsis

These authors searched two databases and reference lists of included papers to identify 20 systematic reviews of observational studies that gave a prevalence of incidental abnormalities (incidentalomas) in patients already being imaged for cancer. Incidentalomas were defined differently across the systematic reviews. CT of the chest resulted in incidentalomas reported in 45% of patients (95% confidence interval [CI], 36% to 55%). The relatively new CT colonoscopy

resulted in incidental findings in 38% of patients (21% to 57%). MRI also reported incidental findings when imaging the spine (22%) and brain (22%). Whole body positron emission tomography (PET) and PET/CT had rates of 2% (95% CI, 1% to 4%). No studies have determined the prevalence of incidentalomas identified via radiography or ultrasonography. Malignancy of incidentalomas were highest with breast findings (42%; 95% CI, 31% to 54%). Renal, thyroid, and ovarian findings were malignant approximately 25% of the time. Extracolonic, prostatic, and colonic incidentalomas were malignant 10% to 20% of the time. Rates of incidentalomas varied substantially among the meta-analyses.

Study design: Systematic review

Funding source: Self-funded or unfunded

Setting: Various (meta-analysis)

Reference: O'Sullivan JW, Muntinga T, Grigg S, Ioannidis JPA. Prevalence and outcomes of incidental imaging findings: umbrella review. *BMJ*. 2018;361:k2387.

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Advance Care Planning Increases Execution of Advance Directives and Surrogate Decision-Maker Assignment

Clinical Question

Does advance care planning lead to increased completion of advance directives and selection of surrogate decision makers among frail older adults?

Bottom Line

In this study, an intensive advance care planning intervention dramatically increased the completion of advance directives and the identification of surrogate decision makers. (Level of Evidence = 2b)

Synopsis

These researchers conducted a cluster randomized trial of facilitated advance care planning education or usual care among modestly frail older adults living in residential care homes or receiving home care nearby. The education intervention included trained facilitators and educational materials

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and tools intended to identify the patients' goals, values, and preferences regarding their health care and to assist in identifying a surrogate decision maker in the event of non-competence. In addition to assigning an activation score (not all that important), the researchers assessed whether the patients had documented their advance care preferences and had selected a surrogate decision maker. The researchers included 16 clusters that contributed 201 patients (between one and 53 patients per cluster). The patients in each group were in their mid-80s and most were female. The intervention patients were more likely to receive home-based care (61%) and to have completed high school (65%) than the control patients (49% and 40%, respectively). At the end of one year, 93% of the intervention group had completed an advance directive compared with 34% of control patients (number needed to treat [NNT] = 2; 95% confidence interval [CI], 2 to 3). Additionally, 94% of the intervention participants had identified a surrogate decision maker compared with 67% of the control patients (NNT = 4; CI, 3 to 6). The consultation sessions took an average of two hours, including travel time, to complete.

Study design: Randomized controlled trial (nonblinded)

Funding source: Foundation

Allocation: Unconcealed

Setting: Other

Reference: Overbeek A, Korfage IJ, Jabbarian LJ, et al. Advance care planning in frail older adults: a cluster randomized controlled trial. *J Am Geriatr Soc.* 2018;66(6):1089-1095.

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Direct Oral Anticoagulants Preferred Over Warfarin for Nonvalvular Atrial Fibrillation in Patients Also Taking Low-Dose Aspirin

Clinical Question

What is the best approach to anticoagulation for patients with nonvalvular atrial fibrillation who also take low-dose aspirin?

Bottom Line

The balance of benefits and harms favors direct oral anticoagulants over warfarin (Coumadin) for patients with nonvalvular atrial fibrillation who require anticoagulation and are already taking low-dose aspirin. It is worth noting that for low-risk patients with nonvalvular atrial fibrillation, aspirin alone is an option. Because these patients were largely taking aspirin as a secondary prevention for cardiovascular disease, edoxaban (Savaysa) was least likely to increase the risk of myocardial infarction. (Level of Evidence = 1a)

Synopsis

Many patients with atrial fibrillation have a separate indication for aspirin. This meta-analysis performed a thorough search of several databases and identified four randomized trials with a total of 21,722 patients who had nonvalvular atrial fibrillation and were taking antiplatelet therapy (most commonly low-dose aspirin) for cardiovascular prevention. Each of the studies randomized patients to receive warfarin or a direct oral anticoagulant such as edoxaban, apixaban (Eliquis), rivaroxaban (Xarelto), or dabigatran (Pradaxa). The studies had between 1.8 and 2.8 years of follow-up. The mean age of included patients was between 70 and 72 years, approximately one-third were women, and between 10% and 55% had experienced a previous stroke. After performing a random effects meta-analysis, the authors found that patients randomized to receive direct oral anticoagulants were less likely to experience a stroke or systemic embolism (hazard ratio [HR] = 0.78; 95% confidence interval [CI], 0.67 to 0.91) or vascular death (HR = 0.85; CI, 0.76 to 0.93) than those randomized to receive warfarin. There was a trend toward a higher risk of myocardial infarction in the direct oral anticoagulant group, primarily driven by the one dabigatran trial (HR = 1.2; CI, 0.97 to 1.4), but a trend toward fewer major hemorrhages with direct oral anticoagulants (HR = 0.83; CI, 0.69 to 1.01). Patients randomized to receive a direct oral anticoagulant were significantly less likely to experience intracranial hemorrhage (HR = 0.38; CI, 0.26 to 0.56). There was minimal to moderate heterogeneity for most outcomes, although the measure used (I²) is unreliable with only four studies.

Study design: Meta-analysis (randomized controlled trials)

Funding source: Foundation

Setting: Outpatient (any)

Reference: Bennaghmouch N, de Veer AJWM, Bode K, et al. Efficacy and safety of the use of non-vitamin K antagonist oral anticoagulants in patients with nonvalvular atrial fibrillation and concomitant aspirin therapy: a meta-analysis of randomized trials. *Circulation.* 2018;137(11):1117-1129.

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Mifepristone Pretreatment Improves Success Rate of Misoprostol for Early Pregnancy Loss

Clinical Question

In women with early pregnancy loss, does pretreatment with mifepristone (Mifeprex) before misoprostol (Cytotec) improve outcomes over treatment with misoprostol alone?

Bottom Line

In women with early pregnancy loss between five and 12 weeks' gestation, pretreatment with 200 mcg of oral

mifepristone before 800 mcg of vaginal misoprostol increases the likelihood of successful expulsion of the gestational sac (number needed to treat [NNT] = 6). (Level of Evidence = 1b-)

Synopsis

The researchers recruited adult women who had a closed cervical os and an ultrasound that showed a nonviable intrauterine pregnancy between five and 12 weeks' gestation. They excluded women with an open cervical os or no visible gestational sac, anemia, a viable or ectopic pregnancy, or any contraindication to the study medications. The mean age of the 300 participants was 30 years, 44% were black, and most had a six- to eight-week gestation. Women were randomized to receive directly observed therapy with oral mifepristone, 200 mcg, followed by 800 mcg of misoprostol (four tablets) inserted vaginally 24 hours later, or to the misoprostol alone. Although women and their physicians were not masked to the treatment assigned, the person assessing the ultrasound was masked. Each woman had a follow-up visit at one to four days, and if a gestational sac was present on the ultrasound, she was offered a second dose of misoprostol or the option of surgical evacuation, with follow-up approximately one week after that. All women had a final follow-up visit at one month. Only seven women were lost to follow-up or withdrew consent in each group. The likelihood of expulsion at the initial follow-up visit was significantly higher with the combination therapy (84% vs. 67%; 95% confidence interval for the difference,

7% to 26%; NNT = 6). Women who did not follow instructions and took the misoprostol fewer than 18 hours after the mifepristone had a somewhat lower likelihood of success (80% vs. 87%; $P = .22$). Among women who had up to two doses of misoprostol, gestational sac expulsion at 30 days was also significantly more likely in the combination therapy group (91% vs. 76%; NNT = 7). Women receiving pretreatment with mifepristone were significantly more likely to experience vomiting (27% vs. 15%; number needed to treat to harm [NNTH] = 8) and headache (59% vs. 48%; NNTH = 9).

Study design: Meta-analysis (randomized controlled trials)

Funding source: Government

Allocation: Concealed

Setting: Various (meta-analysis)

Reference: Schreiber CA, Creinin MD, Atrio J, Sonalkar S, Ratcliffe SJ, Barnhart KT. Mifepristone pretreatment for the medical management of early pregnancy loss. *N Engl J Med*. 2018;378(23):2161-2170.

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Editor's Note: Dr. Mark H. Ebell is Deputy Editor for Evidence-Based Medicine in *AFP* and cofounder and Editor-in-Chief of Essential Evidence Plus, published by Wiley-Blackwell, Inc. Dr. Allen F. Shaughnessy is an Assistant Medical Editor for *AFP*. ■