Breast Cancer Management: New Guidelines, New Recommendations

William C. Dooley, MD, G. Rainey Williams Professor and Chair in Surgical Breast Oncology, and Director of Surgical Oncology, Department of Surgery, University of Oklahoma College of Medicine, Oklahoma City

Survival: breast conservation vs mastectomy — for early-stage breast cancer (BC), 10-yr survival better with breast conservation than with mastectomy; breast conservation more aggressive treatment than mastectomy, and patients more likely to receive National Comprehensive Cancer Network guideline-compliant care; 5-yr survival — “less relevant than ever”; prevention of second malignancy — important to long-term survival in hormone receptor–positive (HR+) BC; use of aromatase inhibitors (AIs) associated with prevention of second BC in 70% to 80% of postmenopausal women

Bilateral mastectomy: disproportionately performed on young women with HR+ BC who are taking no other prevention measures (may be due to, eg, better understanding of reconstruction)

Types of BC: luminal A BC — estrogen receptor–positive (ER+)/progesterone receptor–positive (PR+), human epidermal growth factor receptor 2–negative (HER2–) BC; annual mammography and clinical breast examination (CBE) aimed at detecting luminal A BC; even if 1 or 2 nodes positive, 65% to 75% of patients receive hormone therapy only (no significant difference in survival between women with tumors 1-3 cm in size and women with 0-2 positive nodes); accounts for 65% of all BC; “BC of aging”: late onset of menarche and menopause, and fewer offspring, associated with increased risk; “disease of affluence”; luminal B BC — less common; HR+, HER2+ BC; tends to be faster growing; more likely to be chemotherapy and hormone therapy resistant; failure of detection on mammography slightly more likely; ER-negative (ER–)/PR-negative (PR–)/HER2+ BC — highly sensitive to chemotherapy; with neoadjuvant therapy, pathologic complete response rates of 70% to 80% can be achieved; important to identify patients who are not sensitive to trastuzumab (Herceptin); basal or triple-negative BC (TNBC) — rapidly growing BC (especially in young black women); often associated with BRCA1 mutations; poverty, multiparity, early onset of menarche, and late onset of menopause associated with increased risk

Risk assessment: based on American Cancer Society guidelines published December 2015; average risk — average or less than average risk, and no more than 10% increased risk over national average risk for BC; no concerning history; high risk — 2 breast biopsies, or 1 breast biopsy with proliferative abnormalities; first- or second-degree relative with BC or ovarian cancer; BC survivor

Screening: mammography — women with average risk should start regular screening mammography at 45 yr of age; discuss annual screening with women 40 to 44 yr of age; women 45 to 54 yr of age should be screened annually (supported by “pretty good data”); women ≥55 yr of age can transition to biannual screening (preliminary European studies suggest that mammography identifies only slow-growing BC in older women); screening should continue as long as women in good health and life expectancy ≥10 yr; screening of women with life expectancy <10 yr not strongly supported by data; CBE — not recommended (no modern data on efficacy available)

BC risk: risk for BC diagnosis low in women 40 to 44 yr of age, but increases every year; risk increases from 45 to 49 yr of age, and from 50 to 54 yr of age (absolute 5-yr BC risk similar for each age range); risk decreased in women 40 to 44 yr of age, and markedly decreased in women <40 yr of age; invasive BC — most cases in women ≥45 yr of age; small number of cases seen in women <40 yr of age; risk begins to increase from 40 to 44 yr of age; BC deaths — most deaths in women ≥45 yr of age; peak incidence of life lost from 40 to 65 yr of age; with aging, small group of women have persistent BC risk as their life expectancy decreases (likelihood of dying from BC detected on screening exceedingly low; screening of asymptomatic low-risk women with life expectancy <10 yr not recommended)

False-positive biopsy: ie, positive screening test followed by negative biopsy; 16.3% of patients recalled after first mammography (biopsies performed 2.5% of time); 10-yr cumulative likelihood of false-positive biopsy 7% in women who undergo first annual screening at 40 yr of age (4.8% for biannual screening); likelihood in women 50 yr of age 9.4% (6.4% for biannual screening)

Clinical breast examination: no recent data available; no direct estimates of association with BC mortality; not recommended; study — reviewed 27,000 consecutive CBEs from 2001 to 2013 in high-risk women; score from 0 to 13 given based on findings (eg, discrete and firm masses given score of 4, suspicious axillary lymph nodes given score of 2); total score ≥4 warrants biopsy (probability of BC similar to that indicated by Breast Imaging Reporting and Data System score of 4 or 5); slight increase in detection rate among asymptomatic women at high risk (for average- and low-risk women, “there probably will be very little benefit”); among symptomatic women, positive

Educational Objectives
The goal of this program is to improve management of breast cancer and chronic pain. After hearing and assimilating this program, the clinician will be better able to:
1. Identify risk factors, disease course, and response to treatment associated with different types of breast cancer.
2. Counsel patients about breast cancer screening.
3. List side effects of agents commonly used to treat breast cancer.
4. Develop a curriculum and clinic workflow using a “plan, do, study, act” cycle for the management of chronic pain.
5. Apply lean system concepts to the prescription of analgesic agents.

Faculty Disclosure
In adherence to ACCME Standards for Commercial Support, Audio Digest requires all faculty and members of the planning committee to disclose relevant financial relationships within the past 12 months that might create any personal conflicts of interest. Any identified conflicts were resolved to ensure that this educational activity promotes quality in health care and not a proprietary business or commercial interest. For this program, members of the faculty and planning committee reported nothing relevant to disclose.
predictive value of CBE nearly equal to that of imaging study; analysis found that CBE 81% sensitive and 77% specific, with 10% increase in detection over mammography alone in symptomatic women (>3% increase in asymptomatic women)

**Tamoxifen:** use as hormonal agent more beneficial for 10 yr than for 5 yr; difference in survival not seen until 14 yr (significant difference seen from 14 to 20 yr, and it increases each subsequent year); only hormonal agent for BC in premenopausal women

**Aromatase inhibitors:** in postmenopausal women, AIs more effective than tamoxifen in preventing BC recurrence (50% over 5 yr if taken continuously); associated with joint symptoms and osteoporosis (primarily due to vitamin D deficiency); therapy must be continuous (if AIs interrupted for >1 mo, “clock has to restart” >2 mo for tamoxifen); compliance important; concomitant estrogen or progesterone therapy — topical or systemic use contraindicated in women on AIs due to increased sensitivity (short-term use of, eg, vaginal estrogen in patients on tamoxifen acceptable)

**Trastuzumab:** associated with congestive heart failure (usually detected during active treatment); associated with increased risk for heart disease in subsequent years; screen patients aggressively for heart disease (particularly patients who received radiation therapy over left chest wall); secondary leukemia and lymphoma associated with alkylating agents peak out at 8 to 12 yr, and radiation-induced malignancies peak out at >28 yr

**Paclitaxel** (Eg. Onxol, Paclitaxel Novaplus, Taxol) and docetaxel (Docfrezr, Taxotere): associated with neuropathy; incidence of falls nearly double in BC survivors who received taxane therapy; exercise training for balance (eg, tai chi, yoga) or physical therapy can help decrease risk for falls

**BC recurrence:** brisk walking for >3 hr/wk reduces BC recurrence by 30%; adjuvant chemotherapy reduces BC recurrence by 35%; 60% of women with BC die of heart disease

**Vitamin D:** important for compliance of AIs (eg, anastrozole, letrozole, exemestane); due to loss of enzyme, 75% of population ≥50 yr of age cannot convert prescription vitamin D₃ and D₂ to vitamin D₃ (active form); over-the-counter vitamin D₃ can be dosed directly; calcium interferes with absorption of vitamin D₃; calcium or calcium-containing foods should not be ingested within 2 hr before or after ingestion of oil-based vitamin D capsule); individuals who consume red meat 1 to 2 times per week, or consume milk-derived protein any time during week, do not need additional calcium if level of vitamin D sufficiently high; to prevent joint pain in women on AIs, level of vitamin D₃ should be 60 to 100 ng/mL (in most laboratories, normal range 30-100 ng/mL); no benefit of supplementing patients to 30 to 60 ng/mL; to raise level of vitamin D₃ by 10 points within 3 mo, give 1000 IU/day (ie, to increase level of vitamin D₃ from 20 to 60 ng/mL, give 4000 IU/day); monitor patients; level of vitamin D₃ tends to be low in TNBC and in BC overall; no need to monitor bone density in patients on AIs as long as level of vitamin D₃ >60 ng/mL

**Rebound effects of stopping hormonal therapy:** risk of occult metastasis becomes evident symptomatic increases slightly within 2 yr of discontinuing hormonal therapy (eg, tamoxifen, AIs)

**Clinical pearls:** new guidelines in women at low to average risk; annual mammography recommended in women at above-average risk, positive family history of BC or ovarian cancer, personal history of BC, hyperplasia, atypical high-risk pathology, >2 biopsies in past, or on hormone replacement therapy; CBE and diagnostic mammography primarily recommended in symptomatic women; patients treated with tamoxifen for HR+ BC 15 to 30 yr ago have statistically proven benefit of decreased BC recurrence; treatment with AIs for 5 yr associated with reduction in second BC by 70%

**Questions and answers: inflammatory BC —** most commonly associated with TNBC and HER2+ subtypes; with luminal A BC, prognosis “quite good”; prognosis of HER2+ BC that responds to trastuzumab (especially in neoadjuvant setting) superb; stage at surgery determines outcome; workup of non-fixed, palpable lump in woman <30 yr of age — mammography not useful in women <30 yr of age; ultrasonography diagnostic tool of choice; magnetic resonance imaging (MRI) second-line diagnostic tool (in women >30 yr of age, mammography and ultrasonography diagnostic [MRI second-line diagnostic tool]); vitamin D supplementation — 50,000 IU/wk of vitamin D₃ only beneficial if converted to vitamin D₁ by liver; clinical trials of AIs that have supplemented patients with 60 to 100 ng/mL of vitamin D₃ have failed to show increased risk for calcified arteries (more data needed); decreased efficacy of AIs — studies show that estrogens, obesity, and postmenopausal weight gain decrease efficacy of AIs

**Suggested Readings**


**Chronic Pain Management: Implementing Changes in Primary Care**

Rachel M. Franklin, MD, Professor and Medical Director, Department of Family and Preventive Medicine, University of Oklahoma College of Medicine, Oklahoma City

**History of problem of overprescribing:** in 1990s, pain recognized as “fifth vital sign” by Joint Commission and Veterans Health Administration; many clinicians sued for undertreating pain; oxycodone (OxyContin, Oxycodone, OXa- done) — marketed for noncancer chronic pain; targeted at primary care physicians by drug representatives; marketed as having <1% chance of leading to addiction; by 2003, stock had gone “through the roof”; >50% of prescriptions written by clinicians not trained in chronic pain management; drug manufacturer prosecuted in 2007 (“and now we’re all having to pay the price as a society”); in United States, deaths from accidental drug overdoses of prescription medications outnumber deaths from any other accidental cause

**Development of curriculum:** standardized, evidence-based curriculum for evaluation and management of chronic pain needed; began in January 2012 and continues with combined help of resident physicians, clinic leaders, attorneys, and/or social workers; literature review was conducted, but no good evidence on management of chronic, nonterminal pain was found; improved information processing led to development of curriculum by August 2012

**Development of clinic workflows:** patients informed about new process and guidelines; fundamental goals — patient is center of care in any clinic interaction; quantify pain using, eg, written instruments; standardize histories; emphasize that treatment of chronic, nonterminal pain involves ongoing discussion with patient; goal of pain management not improved pain score, but improved functioning; emphasize multimodal therapy starting with nonpharmacologic therapies, then nonopiate therapies, then trial of opiate therapies (if appropriate); understand mechanism of pain; understand patient’s risk profile; discuss with patient risks, benefits, and tolerability of therapy; help patient set realistic expectations about efficacy and patient’s
responsibilities for care; obtain measurable data based on Pain Disability Index (validated for individual patients; allows physician to monitor patient’s pain score over time); set follow-up goals; emphasize that medication was trial of therapy; be objective; direct conversation toward patient-focused care and safety rather than drug-seeking behavior

**Lean system:** developed by Toyota and originally designed for automobile manufacturing; important to recognize that value of health care services identified by patient; identify steps to, *eg*, refilling medication (eliminating 1-2 steps could improve efficiency); reassessment important; *team-based documentation* — lean concept; data entry performed by clerk rather than physician; focus on delivering value to patients

*Plan, do, study, act* (PDSA) cycle: variant of lean system used in health care; develop plan for change and act on it; be mindful of, *eg*, unintended consequences and/or complications; determine necessary modifications based on information gathered during previous cycle; *example* — start with guidelines or values (*eg*, enhancing patient’s safety and function, providing support to resident physicians); standardize visits; assess function rather than pain score; have patients complete brief pain inventory, then scan and upload into electronic medical record; use opiate risk tool to assess and document risk for diversion, abuse, or misuse of prescription opioids; use CAGE-AID (Adapted to Include Drugs) questionnaire; improve workflows; determine what to measure (*eg*, how many patients on opioids); address inefficiency of patient walk-ins for refills; increase patient satisfaction; *results* — patient satisfaction decreased for ≥3 mo, then increased (“they’ve never been higher”); noncompliant patients and drug misusers, diverters, and sellers were notified that opiates would no longer be prescribed to them, but they would receive multimodal, multidisciplinary care for pain (>10% remained in care, others self-dismissed); resident satisfaction measured every year

**Gathering data and beginning registry:** example — each time patient requests refill of opiate, use form to include patient’s identification information, last appointment date, next appointment date, and whether Oklahoma Bureau of Narcotics and Dangerous Drugs Prescription Monitoring Program (PMP) has been checked; registry allows for alerting schedulers to gather paperwork for folder; use red stamp on checkout form to identify whether patient on chronic opiate analgesia therapy (COAT; triggers workflows in clinic); every appointment scheduled into waiting room in folder; patients informed by letter about changes (*eg*, not prescribing opiate plus anxiolytic, not prescribing >100 mg of morphine equivalent daily) for 3 mo

**Problems:** attending physician unaware of documentation by resident physician in medical record indicating that patient misusing or diverting (leading to refill of prescription); limited medical knowledge of staff about drugs

**Suggested Readings**


**Acknowledgments**

Dr. Dooley and Dr. Franklin were recorded at the 19th Annual Primary Care Update, held May 3-7, 2016, in Midwest City, OK, and presented by the University of Oklahoma College of Medicine. For information about upcoming CME activities from the University of Oklahoma College of Medicine, please visit ouhsc.cloud-cme.com. The Audio Digest Foundation thanks the speakers and the University of Oklahoma College of Medicine for their cooperation in the production of this program.

**Accreditation:** The Audio Digest Foundation is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

**Designation:** The Audio Digest Foundation designates this enduring material for a maximum of 2 AMA PRA Category 1 Credits™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

The American Academy of Physician Assistants (AAPA) accepts certificates of participation for educational activities designated for AMA PRA Category 1 Credit™ from organizations accredited by ACCME or a recognized state medical society. Physician assistants may receive a maximum of 2 AAPA Category 1 CME credits of each Audio Digest activity completed successfully.

This Enduring Material series activity, *Audio Digest Family Medicine* Volume 65, from 01/01/2017 - 12/31/2017, has been reviewed and is acceptable for credit by the American Academy of Family Physicians. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

Audio Digest Foundation is accredited as a provider of continuing nurse practitioner education by the American Academy of Nurse Practitioners (AANP Approved Provider number 030904). Audio Digest designates each activity for 2.0 CE contact hours, including 0.5 pharmacology CE contact hours.

The California State Board of Registered Nursing (CA BRN) accepts courses provided for AMA PRA Category 1 Credit™ as meeting the continuing education requirements for license renewal.

**Expiration:** This CME activity qualifies for AMA PRA Category 1 Credit™ for 35 months from the date of publication.

**Cultural and linguistic resources:** In compliance with California Assembly Bill 1195, Audio Digest Foundation offers selected cultural and linguistic resources on its website. Please visit this site: www.audiodigest.org/CLCResources.

**Estimated time to complete the educational process:**

| Review Educational Objectives on page 1 | 5 minutes |
| Take pretest | 10 minutes |
| Listen to audio program | 60 minutes |
| Review written summary and suggested readings | 35 minutes |
| Take posttest | 10 minutes |
1. Which of the following statements about breast cancer survival is true?
   (A) For early-stage breast cancer, 10-year survival is better with breast conservation than with mastectomy
   (B) Mastectomy is a more aggressive form of treatment than breast conservation
   (C) For early-stage breast cancer, 5-year survival is more relevant than 10-year survival
   (D) A and B

2. Which of the following is associated with increased risk for triple-negative breast cancer?
   (A) Affluence
   (B) Multiparity
   (C) Late onset of menarche
   (D) Early onset of menopause

3. According to American Cancer Society screening guidelines, women can transition from annual mammography to biannual mammography if they are at least:
   (A) 45 yr of age
   (B) 55 yr of age
   (C) 65 yr of age
   (D) 75 yr of age

4. Which of the following statements about clinical breast examination is true?
   (A) Recommended in high-risk women >60 yr of age
   (B) Shown to decrease breast cancer mortality in younger women
   (C) More useful in asymptomatic women than in symptomatic women
   (D) Not recommended due to lack of data

5. The use of aromatase inhibitors is associated with which of the following complications?
   (A) Hearing loss
   (B) Hypertension
   (C) Loss of bone density
   (D) Irritable bowel syndrome

6. Which of the following breast cancer agents is associated with an increased risk for congestive heart failure?
   (A) Trastuzumab
   (B) Paclitaxel
   (C) Docetaxel
   (D) Tamoxifen

7. Which of the following is the diagnostic tool of choice for a woman <30 yr of age with a nonfixed, palpable lump?
   (A) Magnetic resonance imaging
   (B) Ultrasonography
   (C) Mammography
   (D) Chest x-ray

8. Which of the following statements about oxycodone is true?
   (A) Initially marketed for chronic pain associated with cancer
   (B) Marketed as having a <1% chance of leading to addiction
   (C) Targeted mainly at chronic pain specialists by drug representatives
   (D) Temporarily taken off the market in 2003

9. Which of the following is a goal of a clinical workflow for chronic pain management?
   (A) Improving a patient’s pain score
   (B) Starting multimodal therapy with a trial of opiates
   (C) Pointing out drug-seeking behavior
   (D) Improving a patient’s functioning

10. Which of the following is an example of a lean system–based concept in chronic pain management?
    (A) Allowing walk-ins for opiate refills
    (B) Eliminating the use of questionnaires (eg, CAGE-AID [Adapted to Include Drugs])
    (C) Implementing team-based documentation (eg, data entry performed by clerk rather than physician)
    (D) Setting high expectations of treatment

Answers to Audio Digest Family Medicine Volume 65, Issue 04: 1-D, 2-B, 3-A, 4-C, 5-A, 6-B, 7-A, 8-C, 9-D, 10-A