



Older breast cancer undertreatment: unconscious bias to undertreat – potential role for the international geriatric radiotherapy group?

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Abstract: The prevalence of breast cancer increases with age. Older breast cancer patients often present with locally advanced disease at presentation because mammography, which diagnosed early stage disease, is not recommended after the age of 75. In addition, they are often undertreated even when they are physically fit and have non-metastatic disease. As a result, survival is often poor. Physicians bias may be a factor in their undertreatment and lack of representation in prospective clinical trials. Physicians should be educated that chronological age is not a contraindication to curative treatment for older breast cancer patients. As a research group devoted to older cancer patients, women, and minorities, the International Geriatric Radiotherapy Group (IGRG) plans to conduct prospective trials to assess biomarkers for frailty, the controversial issue of mammography for older breast cancer patients, and the incorporation of frailty index for curative breast cancer treatment. The data obtained may help to decrease physician bias and to establish future guidelines for older breast cancer patients treatment.

Keywords: Elderly; breast cancer; undertreatment; discrimination

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Introduction

The prevalence of breast cancer increases with age. It is estimated that 67% of breast cancer will develop in women 65 years and older (1). Older breast cancer tumor biology is often slow growing with a good molecular profile including the expression of estrogen (ER) and progesterone (PR) receptors (2). Thus, if diagnosed early and if treated properly, older breast cancer patients should have comparable or better survival compared to

younger patients with a more aggressive tumor biology (3). However, most studies on older breast cancer patients reported a poorer outcome compared to younger patients (4-6). The management of older breast cancer patient is complex. Older patients tend to have multiple co-morbidity with advanced age which may preclude curative treatment or may have contributed to their poor survival (7-9). On the other hand, physically fit individuals who have localized disease may have a poor survival if they are not treated

properly and/or cancer diagnosis is delayed until the disease is locally advanced or metastatic. Undertreatment of older patients with breast cancer has been reported in many studies and may have contributed to their low survival rates (10-17). Omission of surgery, sentinel lymph node dissection, radiotherapy, and adjuvant chemotherapy are frequently reported among older breast cancer patients (14-17). Physicians attitude in the management of older breast cancer patients which may be perceived as discrimination has been implicated as one of the potential cause for their substandard treatment (18,19).

Thus, an understanding of the factors which may influence physicians management of older breast cancer patients may potentially improve their care and may provide guidelines to help the clinicians involved in their care. As an international research group devoted to the care of older people, minorities and women with cancer, the International Geriatric Radiotherapy Group (IGRG) (<http://www.igr.org>) may play a potential role to solve those issues.

The role of mammogram in older cancer patients

Screening mammography has been effective to diagnose breast cancer at an early stage in women 50 years old or older and reduce cancer mortality (20). However, current recommendations set the upper age limit for screening mammogram as 75 years old (21-23). Because of the lack of randomized studies, the benefits of screening mammogram in patients older than 75 remain unproven. However, preliminary studies suggested that as the frequency of screening mammogram decreased among older patients, the prevalence of clinically palpable breast cancer increased significantly, leading to a higher risk of cancer death (24).

In addition, among older women who were diagnosed with cancer through mammography, the ones who had frequent sequential mammograms had a better prognosis because their cancer were diagnosed at an early stage (25). The benefits of frequent sequential mammography among patients 75 years old or older were also corroborated in another study as patients who had mammography performed within a shorter interval had a better survival compared to the ones with a longer period (26). In that study, patients who had mammograms performed at a longer interval presented with locally advanced disease at diagnosis and their tumor were biologically more aggressive. Other studies also corroborated the survival benefit of performing frequent mammography in older patients (27-29). In addition to improved life expectancy, mammography for older patients may also be cost-effective (30).

Unfortunately, it is difficult to make a definite conclusion on the benefits of mammography in older cancer patients since none of those studies were randomized. As most randomized studies specifically excluded the inclusion of older cancer patients, there may be a systemic bias among physicians who designed those studies (31).

Surgery for older breast cancer patients

Surgery remains the corner stone for older breast cancer with localized disease. For selected patients, postoperative mortality was low and survival rates similar to younger patients (3,32). A recent review of the Surveillance, Epidemiology, and End Results (SEER) database of 13,007 breast cancer patients older than 80 years demonstrated better survival and cancer specific survival among patients undergoing surgery compared to the ones with no surgery (33). Another study corroborated the survival advantage of having surgery in that patient population (34). Thus, physically fit breast cancer patients with localized disease should undergo surgery regardless of their chronological age. However, surgical omission for older breast cancer patients remains prevalent. As an illustration, among 23,961 patients with breast cancer older than 70 years and diagnosed at an early stage, 46.1% had endocrine therapy instead of surgery (35). Their survival was significantly decreased compared to the ones who underwent surgery (35).

Omission of surgery ranged from 2.5–24.2% and 4.6–50.8% for stage I and stage III disease respectively for breast cancer patients 70 years old or older (36).

Non-surgical treatment increased with patient age and was worst in patients 80 years or older (37). Among older breast cancer patients who did undergo surgery, axillary lymph node dissection were frequently not performed leading to under staging and undertreatment (13,38). Chronological age and presence of multiple comorbidities were often cited as the rationale for incomplete axillary staging (39). Surgery undertreatment was further compounded by the lack of adjuvant radiotherapy and/or chemotherapy in breast cancer patients 70 years or older resulting in poor survival for those patients (40).

Radiotherapy for older cancer patients

The advent of modern radiotherapy technique allows completion of a short treatment course within one to four weeks for older cancer patients with minimal morbidity (41-48). Excellent loco-regional and survival with acceptable

complications were reported. In addition, in selected patients, accelerated partial breast irradiation (APBI) offered the convenience of finishing treatment within a week, thus, minimizing the challenge of daily transportation if the patients were to undergo a conventional six weeks course of radiotherapy (48). As a result, it is very difficult to justify the omission of radiotherapy after breast conservation surgery or total mastectomy if radiotherapy is indicated.

In reality, radiotherapy is routinely denied to older breast cancer patients following surgery regardless of the stage (40,49-68). The percentage of patients not receiving radiotherapy after surgery increased with patient age. Patients who were 80 years old or older were most affected. The percentage of patients who did not receive radiotherapy after breast conservative surgery (BCS) in that age group ranged from 26% to 89% (40,49,63,64,66). Overall, administration of radiotherapy was associated with a lower rate loco-regional recurrence, and a decreased risk of salvage mastectomy for early stage breast cancer. In selected groups of patients, a survival advantage was also reported among the patients who received radiotherapy (40,49,50,55,57,59,67). The survival benefit was most pronounced among patients ER and PR negative tumors, metaplastic and large tumors (49,55,59,68).

There are several possible reasons for the omission of radiotherapy following BCS. One of them is the Cancer and Leukemia Group B (CALGB) 9,343 report of the lack of survival benefit among older breast cancer women with small, ER and PR positive tumors who underwent adjuvant radiotherapy following BCS compared to the ones receiving Tamoxifen alone (69).

In another study, the most common reason cited for omission of radiotherapy was physician recommendation against its administration (53). However in that study, comorbidity factors did not influence physicians decisions but chronological age was the deciding factor (53).

Corroborating physician bias, Downs-Canner *et al.* (63) reported that patient estimated risk of death in 10 years was not a factor in physicians' decision about delivering radiotherapy to older patients with small ER, PR positive tumors after BCS (63). In fact, there was a wide variation among institutions about the decision whether or not to omit radiotherapy for older patients whose tumors fulfill those criteria (56). Omitting radiotherapy for selected older patients remains a controversial issue among cancer physicians because of the high rate of long-term recurrence among patients receiving Tamoxifen only. Hughes *et al.* (70) reported a 10-year local recurrence rate of 9% and 2%

among patients who had Tamoxifen only and postoperative irradiation as a follow-up of CALGB 9343. The patients who recurred had to undergo salvage mastectomy which may affect their quality of life. Taken together, those studies suggested that physicians decision to omit radiotherapy following BCS were subjective and not based on objective parameters such as frailty index which may impact patient long-term survival (71).

Chemotherapy for older breast cancer patients

Even though the data is sparse, preliminary studies suggested that physically fit older breast cancer patients tolerated chemotherapy quite well. In a survey of 1,280 non-metastatic breast cancer patients 65 years old or older, 76% were considered robust (71). Compared to frail patients, they were able to tolerate chemotherapy and hormone therapy better and had better cancer-specific survival (71). In another study, patients who were 70 years old or older had similar disease free survival compared to younger patients when they underwent adjuvant chemotherapy after surgery for breast cancer despite a higher disease burden and a higher prevalence of co-morbidity (72). Other studies also corroborated the survival advantage of older fit breast cancer patients who received adjuvant chemotherapy (73-75). The benefit of chemotherapy was most pronounced among patients at higher risk of recurrences such as large tumors, axillary lymph nodes involvement and hormonal negative breast cancer (76). Thus, older fit women with breast cancer should receive chemotherapy when indicated to decrease recurrence risk and to improve their survival odds.

Omission of chemotherapy because of chronological age is a worldwide phenomenon. In the Netherlands and Ireland for example, only 6% and 24% of patients 65 years old or older received chemotherapy respectively for stage I-III breast cancer (77). In Japan, the corresponding figures were 36% and 15% for the age group 65-75 and over 75 years old respectively (54). In Germany, non-adherence to chemotherapy also increased with age as only one out of 42 patients 80 years old or older received chemotherapy (40). In the United States (US), among 5,081 women 66 years old and older who had ER and PR negative breast cancer, only 34% received chemotherapy (78). Administration of chemotherapy was associated with a 15% in reduction of breast cancer mortality for those patients (78). Similar omission of chemotherapy and subsequent reduction of survival rate with advanced chronological age was also

reported among breast cancer patients in Georgia (79). Thus, older breast cancer patients face challenge regardless of the geographic location.

Physicians attitude toward older breast cancer patients

Age bias has been recognized as one of the cause of underutilization of BCS in older breast cancer patients. In a survey of medical and surgical residents, modified radical mastectomy (MRM) was recommended for 38% of patients older than 59 years old compared to 11% for patients less than 31 years old even though the residents were instructed that MRM and BCS had similar outcome before the survey (80). As a result, it is not surprising that BCS rates decreased significantly with chronological age across the United States (81). This age bias is also reflected nationally through the underrepresentation of older breast cancer patients in clinical trials. For example, only 9% of patients were 65 years or older in 164 Southwest Oncology group breast cancer trials between 1993 and 1996 (82). This age based disparity was still persistent in breast cancer clinical trials between 2000 and 2002 (83). At the last update in 2016, according to the US Food and Drug Administration (FDA), only 4% of women with breast cancer older than 75 was recruited in US clinical trials (84). Thus, unless clinicians make a conscious effort to design and recruit older women in breast cancer clinical trials, those patients will continue to be undertreated because of the lack of data.

One of the possible cause for under representation of older breast cancer patients in clinical trials is the physician belief that older patients may be unable to tolerate treatment in addition to the lack of data to guide optimal treatment. Foster *et al.* (18) reported the survey of 200 medical oncologists who were given two scenarios of two patients of stage IIA breast cancer with excellent performance status but different age. Ninety three percent of those surveyed recommended adjuvant chemotherapy for the 63 years old patient. However, only 66% would recommend similar therapy if the patient was 75 years old even in the absence of comorbidity. Another survey of medical oncologists about treatment recommendation for breast cancer patients also corroborated the omission of chemotherapy based on patient chronological age (19). Morrow *et al.* (85) also reported that physicians belief was most likely the cause for omission of surgery for older breast cancer patients. There were two groups of older breast cancer patients with almost identical disease stage

and comorbidity factors, in two different cancer treatment units. The physicians who recommended surgery more frequently in one unit instead of endocrine therapy believed that their patients could tolerate anesthesia and the surgical procedure (85). Thus, physicians education may be the key to change their attitude toward older patients with breast cancer.

Potential role of the International Geriatric Radiotherapy Group to minimize bias and to improve the care of older breast cancer patients

As an international organization of over 1,000 institutions in 123 countries devoted to the care of older cancer patients, minorities, and women, the IGRG is well positioned to address the issue of bias and discrimination against older cancer patients. Following our workshop in Barcelona in 2018 and the University of Umea presentation in 2019, we identified critical issues affecting the care of older cancer patients and proposed potential solutions (86). For instance, the upper age limit for screening mammography needs to be revised for early diagnosis of breast cancer for older patients. New biomarkers for frailty such as urinary 8-oxo-7, 8-dihydroguanosine (8-oxoGsn) needs to be investigated to assess patient physiologic age (87). Future prospective studies for older breast cancer patients should be conducted by a team of physicians and scientists who are familiar with the care of older cancer patients. Co-morbidity factors and frailty index should be incorporated in those studies such as physiological age instead of chronological age is the main determinant for curative treatment. The data obtained will demonstrate and allay the fear of physicians that physically fit older breast cancer patients tolerate curative treatment as well as younger patients. In a review of the role of physicians bias toward making improper treatment decision, acknowledging bias may be the first step to decrease undertreatment of older breast cancer patients and to improve their empathy for this segment of the patient population (88).

Conclusions

Older breast cancer patients face discrimination because of their chronological age. Current policy of cancer screening does not encourage mammography after the age of 75. Older breast cancer patients are frequently excluded from current clinical prospective trials and are undertreated subsequently leading to a poor survival. Physicians bias may play a role in the undertreatment of this patient population.

Physicians need to be educated that chronological age is not a contraindication to curative treatment. The IGRG plans to conduct prospective studies in the future to improve the quality of care of older breast cancer patients.

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References

- Smith BD, Smith GL, Hurria A, et al. Future of cancer incidence in the United States: Burdens upon an aging, changing nation. *J Clin Oncol* 2009;27:2758-65.
- Syed BM, Green AR, Paish EC, et al. Biology of primary in older women treated by surgery with correlation with long-term clinical outcome and comparison with their younger counterparts. *Br J Cancer* 2013;108 1042-51.
- Reddy A, Mullapudi NA, Kabeer KK, et al. Treatment of elderly breast cancer patients in a breast center in India. *Indian J Cancer* 2019;56:45-9.
- Kim JY, Kang D, Nam SJ, et al. Clinical features and outcomes of invasive breast cancer: Age specific analysis of a modern hospital based registry. *J Glob Oncol* 2019;5:1-9.
- Bastiaannet E, Portielle JE, van de Velde CJ, et al. Lack of survival gain for elderly women with breast cancer. *Oncologist* 2011;16:415-23.
- Brandt J, Garne JP, Tengrup I, et al. Age at diagnosis in relation to survival following breast cancer: a cohort study. *World J Surg Oncol* 2015;13:33.
- Gironés R, Torregrosa D, Diaz-Beveridge R. Comorbidity, disability and geriatric syndromes in elderly breast cancer survivors. *Crit Rev Oncol Hematol* 2010;73:236-45.
- Wasif N, Neville M, Gray R, et al. Competing risk of death in elderly patients with newly diagnosed stage I breast cancer. *J Am Coll Surg* 2019;229:30-36.e1.
- Clough-Gorr KM, Stuck AE, Thwin SS, et al. Older breast cancer survivors: geriatric assessment domains are associated with poor tolerance of treatment adverse effects and predict mortality over 7 years follow-up. *J Clin Oncol* 2010;28:380-6.
- Wheeler SB, Carpenter R, Peppercorn J, et al. Predictors of timing of adjuvant chemotherapy in older women with hormone receptor negative, stage II, III breast cancer. *Breast Cancer Res Treat* 2012;131:207-16.
- Schonberg MA, Marcantonio ER, Li D, et al. Breast cancer among the oldest old: Tumor characteristics, treatment choices, and survival. *J Clin Oncol* 2010;28:2038-45.
- Silliman RA. When cancer in older adults is undermanaged: the breast cancer patient story. *J Am Geriatr Soc* 2009;57:S259-261.
- Malik MK, Tartter PI, Belfer R. Undertreated breast cancer in the elderly. *J Cancer Epidemiol* 2013;2013:893104.
- Reeder-Hayes KE, Bainbridge J, Meyer AM, et al. Race and age disparities in receipt of sentinel lymph nodes biopsy for early stage breast cancer. *Breast Cancer Res Treat* 2011;128:863-71.
- Wink CJ, Woensdregt K, Nieuwenhuijzen GAP, et al. Hormonal treatment without surgery for patients aged 75 years or older with operable breast cancer. *Ann Surg*

- Oncol 2012;19:1185-91.
16. Wang H, Singh AP, Luce SAS, et al. Breast cancer treatment practices in elderly women in a community hospital. *Int J Breast Cancer* 2011;2011:467906.
 17. Cyr A, Gillanders WE, Aft RL, et al. Breast cancer in elderly women (>80): Variation in standard of care. *J Surg Oncol* 2011;103:201-6.
 18. Foster JA, Salinas GD, Mansell D, et al. How does older age influence oncologists' cancer treatment. *The Oncologist* 2010;15:584-92.
 19. Protière C, Viens P, Rousseau F, et al. Prescribers' attitude toward elderly breast cancer patients. Discrimination or empathy. *Crit Rev Oncol Hematol* 2010;75:138-50.
 20. Myers ER, Moorman P, Gierisch JM, et al. Benefits and harms of breast cancer screening. *JAMA* 2015;314:1615-34.
 21. Siu AL. Screening for breast cancer: U.S. Preventive services task force recommendation statement. *Ann Int Med* 2016;164:279-96.
 22. Wilt TJ, Harris RP, Qaseem A. Screening for cancer: advice for high value care from the American College of Physicians. *Ann Int Med* 2015;162:718-25.
 23. Sardanelli F, Aase HS, Alvarez M, et al. Position paper on screening for breast cancer by the European Society for Breast Imaging (EUSOBI) and 30 breast radiology body from Austria, Belgium, Bosnia and Herzegovina, Bulgaria, Croatia, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Israel, Lithuania, Moldavia, The Netherlands, Norway, Poland, Portugal, Romania, Serbia, Slovakia, Spain, Sweden, Switzerland, and Turkey. *Eur Radiol* 2017;27:2737-43.
 24. Vacek PM, Skelly JM. A prospective study of the use and effects of screening mammography in women age 70 and older. *J Am Geriatr Soc* 2015;63:1-7.
 25. Vyas A, Madhavan S, Sambamoorthi U. Association of persistence with mammography screening and stage at diagnosis among elderly women diagnosed with breast cancer. *Breast Cancer Res Treat* 2014;148:645-54.
 26. Simon MS, Wassertheil-Smoller S, Thomson CA, et al. Mammography interval and breast cancer mortality in women over the age of 75. *Breast Cancer Res Treat* 2014;148:187-95.
 27. Van Dijk JA, Verbeek AL, Beex LV, et al. Mammographic screening after the age of 65 years: evidence for a reduction in breast cancer. *Int J Cancer* 1996;66:727.
 28. Sanderson M, Levine RS, Fadden MK, et al. Mammography screening among the elderly: a research challenge. *Am J Med* 2015;128:1362.e7-14.
 29. Braithwaite D, Walter LC, Izano M, et al. Benefits and harms of screening mammography by comorbidity and age; a qualitative synthesis of observational studies and decision analyses. *J Gen Intern Med* 2016;31:561-72.
 30. Kerlikowske K, Salzman P, Phillips KA, et al. Continuing screening mammography in women age 70 to 79 years: impact on life expectancy and cost-effectiveness. *JAMA* 1999;282:2156-63.
 31. Marosi C, Köller M. Challenge of cancer in the elderly. *ESMO open* 2016;1:e000020.
 32. Herbsman H, Feldman J, Seldera J, et al. Survival following breast cancer surgery in the elderly. *Cancer* 1981;47:2358-63.
 33. Wang Z, Zhou Z, Li W, et al. Treatment strategies and predicting prognoses in elderly patients with breast cancer. *Cancer Manag Res* 2018;10:3207-18.
 34. Ojala K, Meretoja TJ, Mattson J, et al. Surgical treatment and prognoses of breast cancer in the elderly. *Eur J Surg Oncol* 2019;45:956-62.
 35. Ward SE, Richards PD, Morgan JL, et al. Omission of surgery in older women with early breast cancer has an adverse effect on breast cancer specific survival. *Br J Surg* 2018;105:1454-63.
 36. Derks MGM, Bastiaannet E, Kiderlen M, et al. Variation in treatment and Survival of older patients with non-metastatic breast cancer in five European countries: a population-based study from the EURECCA breast cancer group. *Br J Cancer* 2018;119:121-9.
 37. Hamaker ME, Bastiaannet E, Evers D, et al. Omission of surgery in elderly patients with early stage breast cancer. *Eur J Cancer* 2013;49:545-52.
 38. Litvak DA, Arora R. Treatment of elderly breast cancer patients in a community hospital setting. *Arch Surg* 2006;141:985-90; discussion 990.
 39. Poodt IGM, Schipper RJ, Vugts G, et al. The rationale for and long-term outcome of incomplete axillary staging in elderly women with primary breast cancer. *Eur J Surg Oncol* 2018;44:1714-9.
 40. Hancke K, Denking MD, König J, et al. Standard treatment of female patients with breast cancer decreases substantially for women age 70 years and older: a German clinical cohort study. *Ann Oncol* 2010;21:748-53.
 41. Doré M, Cutuli B, Cellier P, et al. Hypofractionated irradiation in elderly patients with breast cancer after breast conservative surgery and mastectomy: Analysis of 205 cases. *Radiat Oncol* 2015;10:161.
 42. De Santis MC, Bonfantini F, Di Salvo F, et al. Hypofractionated whole breast irradiation with or without

- boost in elderly patients: Clinical evaluation of an Italian experience. *Clin Breast Cancer* 2018;18:e1059–e1066.
43. Cante D, Franco P, Sciacero P, et al. Hypofractionated whole breast radiotherapy and concomitant boost after breast conservation in elderly patients. *Tumori* 2016;102:196–202.
 44. Jacobs DHM, Speijer G, Petoukhova AL, et al. Acute toxicity of intraoperative radiotherapy and external beam accelerated partial breast irradiation in elderly breast cancer patients. *Breast Cancer Res Treat* 2018;169:549–59.
 45. Hannoun-Lévi JM, Cham Kee DL, Gal J, et al. Accelerated partial breast Irradiation for suitable elderly women using a single fraction of multicatheter interstitial high dose rate brachytherapy: early results of single fraction elderly breast irradiation (SIFEBI) phase I/II trial. *Brachytherapy* 2018;17:407–14.
 46. Sumodhee S, Levy J, Chamorey E, et al. Accelerated partial breast irradiation for elderly women with early breast cancer: a compromise between whole breast irradiation and omission of radiotherapy. *Brachytherapy* 2017;16:929–34.
 47. Meattini I, Saieva C, Marrazzo L, et al. Accelerated breast irradiation using intensity-modulated radiotherapy technique compared to whole breast irradiation for patients age 70 or older: subgroup analysis from a randomized phase III trial. *Breast Cancer Res Treat* 2015;153:539–47.
 48. Genebes C, Chand ME, Gal J, et al. Accelerated partial breast irradiation in the elderly: 5-year results of high dose rate multi-catheter brachytherapy. *Radiat Oncol* 2014;9:115.
 49. Haque W, Verma V, Butler EB, et al. Omission of radiotherapy in elderly women with early stage metaplastic breast cancer. *Breast* 2018;38:154–9.
 50. Herskovic AC, Wu X, Christos PJ, et al. Omission of adjuvant radiotherapy in the elderly breast cancer patient: missed opportunity? *Clin Breast Cancer* 2018;18:418–31.
 51. Haque W, Verma V, Hsiao KY, et al. Omission of radiotherapy following breast conservation in older (>70 years) women with T1-T2N0 triple-negative breast cancer. *Breast J* 2019. [Epub ahead of print].
 52. Wu SG, Zhang WW, Sun JY, et al. Omission of postoperative radiotherapy in women age 65 or older with tubular carcinoma of the breast after breast conservative surgery. *Front Oncol* 2018;8:190.
 53. Shumway DA, Griffith KA, Hawley ST, et al. Patient views and correlate of radiotherapy emission in a population-based sample of older patients with favorable prognosis breast cancer. *Cancer* 2018;124:2714–23.
 54. Yamada A, Narui K, Sugae S, et al. Operation with less adjuvant therapy for elderly breast cancer. *J Surg Res* 2016;204:410–7.
 55. Eaton BR, Jiang R, Torres MA, et al. Benefit of adjuvant radiotherapy after breast conservative therapy among elderly women with T1-T2N0 estrogen negative breast cancer patients. *Cancer* 2016;122:3059–68.
 56. McCormick B, Ottersen RA, Hughes ME, et al. Impact of guideline changes on use or omission of radiation in the elderly with early breast cancer: practice patterns at National Comprehensive Cancer Network. *J Am Coll Surg* 2014;219:796–802.
 57. Badakhshi H, Gruen A, Sehoul J, et al. The impact of patient compliance with adjuvant radiotherapy: a comprehensive cohort study. *Cancer Med* 2013;2:712–7.
 58. Vrana D, Gatek J, Lukesova L, et al. Omission of adjuvant radiation therapy in elderly patients with low risk breast cancer undergoing breast conservative surgery—two centers experience. *Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub* 2014;158:461–4.
 59. Shen X, Anne PR, Keith SW, et al. Radiation therapy use and outcomes among older women with ER-positive and ER-negative stage I breast cancer. *Am J Clin Oncol* 2014;37:241–7.
 60. Showalter SL, Grover S, Sharma S, et al. Factors influencing surgical and adjuvant therapy in stage I breast cancer: a SEER 18 database analysis. *Ann Surg Oncol* 2013;20:1287–94.
 61. Williams LJ, Kunkler IH, King CC, et al. A randomized controlled trial of postoperative radiotherapy following breast conservative surgery in a minimum risk population. Quality of life at 5 years in the PRIME trial. *Health Technol Assess* 2011;15:i-xi, 1–57.
 62. Valassiadou K, Morgan DA, Robertson JE, et al. Successful management of elderly breast cancer patients treated without radiotherapy. *World J Surg Oncol* 2007;5:62.
 63. Downs-Canner S, Zabor EC, Wind T, et al. Radiation therapy after breast conservative surgery in women 70 years of age and older: how wisely do we choose? *Ann Surg Oncol* 2019;26:969–75.
 64. Pollock YG, Blackford AL, Jeter SC, et al. Adjuvant radiation use in older women with early stage breast cancer at John Hopkins. *Breast Cancer Res Treat* 2016;160:291–6.
 65. Rhieu BH, Rajagopalan MS, Sukumvanich P, et al. Patterns of care for omission of radiation therapy for elderly women with early stage breast cancer receiving hormonal therapy. *Pract Radiat Oncol* 2015;5:e267–73.
 66. Corradini S, Niyazi M, Niemoeller OM, et al. Adjuvant

- radiotherapy after breast conservative surgery—a comparative effective research study. *Radiother Oncol* 2015;114:28-34.
67. Truong PT, Berstein V, Lesperance M, et al. Radiotherapy omission after breast conservative surgery is associated with reduced breast cancer-specific survival in elderly women with breast cancer. *Am J Surg* 2006;191:749-55.
 68. Martelli G, Boracchi P, Guzzetti E, et al. Omission of radiotherapy in elderly patients with early breast cancer: 15-Year results of a prospective non-randomised trial. *Eur J Cancer* 2015;51:1358-64.
 69. Palta M, Palta P, Bhavsar NA, et al. The use of adjuvant radiotherapy in elderly patients with early stage breast cancer: changes in practice patterns after publication of Cancer and Leukemia Group B 9343. *Cancer* 2015;121:188-93.
 70. Hughes KS, Schnaper LA, Bellon JR, et al. Lumpectomy plus Tamoxifen with or without irradiation in women age 70 years or older with early breast cancer: Long-term follow-up of CALGB 9343. *J Clin Oncol* 2013;31:2382-7.
 71. Mandelblatt JS, Cai L, Luta G, et al. Frailty and long-term mortality of older breast cancer patients: CALGB 369901 (Alliance). *Breast Cancer Res Treat* 2017;164:107-17.
 72. Fietz T, Zahn M, Kohler A, et al. Routine treatment and outcome of breast cancer in younger versus elderly patients: results from the Senora project of the prospective German TMK cohort study. *Breast Cancer Res Treat* 2018;167:567-78.
 73. Muss HB, Berry DA, Cirincione CT, et al. Adjuvant chemotherapy in older patients with early stage breast cancer. *N Engl J Med* 2009;360:2055-65.
 74. Muss HB, Woolf S, Berry D, et al. Adjuvant chemotherapy in older and younger women with lymph node positive breast cancer. *JAMA* 2005;293:1073-81.
 75. Du XL, Jones DV, Zhang D. Effectiveness of adjuvant chemotherapy for node Positive operable breast cancer in older women. *J Gerontol A Biol Sci Med Sci* 2005;60:1137-44.
 76. Ward SE, Holmes GR, Ring A, et al. Adjuvant chemotherapy for breast cancer in older women: an analysis of retrospective English cancer registration data. *Clin Oncol (R Coll Radiol)* 2019;31:444-52.
 77. Kiderlen M, Walsh PM, Bastiannet E, et al. Treatment strategies and survival of older breast cancer patients—an international comparison between the Netherlands and Ireland. *PLoS One* 2015;10:e0118074.
 78. Elkin EB, Hurria A, Mitra N, et al. Adjuvant chemotherapy and survival in older women with hormone negative breast cancer: assessing outcome in a population based, observational cohort. *J Clin Oncol* 2006;24:2757-64.
 79. Vashakidze N, Mebonia N, Gvamichava R. Effect of age at diagnosis on the prognoses in female breast cancer patients in Georgia. *Georgian Med News* 2018;284:27-32.
 80. Madan AK, Aliabadi-Wahle S, Beech DJ. Age bias: a cause of underutilization of breast conservative treatment. *J Cancer Educ* 2001;16:29-32.
 81. Alderman AK, Bynum J, Sutherland J, et al. Surgical treatment of breast cancer among the elderly in the United States. *Cancer* 2011;117:698-704.
 82. Hutchins LF, Unger JM, Crowley JJ, et al. Underrepresentation of patients 65 years old or older in cancer treatment trials. *N Engl J Med* 1999;341:2061-7.
 83. Murthy VH, Krumholz HM, Gross CP. Participation in cancer clinical trials: Race, sex, and age disparities. *JAMA* 2004;291:2720-6.
 84. Kanapuru B. Enrollment of older adults in cancer clinical trials: US Food and Drug administration experience. *FDA*.
 85. Morrow ES, Dolan RD, Doughty J, et al. Variation in the management of elderly patients in two neighboring breast units is due to preferences and attitudes of health professionals. *Breast Cancer (Dove Med Press)* 2019;11:179-88.
 86. Popescu T, Karlsson U, Vinh-Hung V, et al. Challenges facing radiation oncologists in the management of older cancer patients: consensus of the International Geriatric Radiotherapy Group. *Cancers* 2019;11:371.
 87. Gan W, Liu XL, Yu T, et al. Urinary 8-oxo-7,8-dihydroguanosine as a potential biomarker for aging. *Front Aging Neurosci* 2018;10:34.
 88. Chapman EN, Kaatz A, Carnes M. Physicians and implicit bias: how doctors may unwittingly perpetuate health care disparity. *J Gen Intern Med* 2013;28:1504-10.

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