# newsround

## Selected reports edited by Janet Fricker

### Optimal time for initiation of adjuvant chemotherapy according to subtype

■ Journal of Clinical Oncology

Time delays in initiation of adjuvant chemotherapy have an adverse effect on outcomes for breast cancer patients with stage II and III disease, triple-negative tumours and HER2-positive tumours treated with trastuzumab, a single-institution retrospective cohort study has found.

Randomised clinical trials have shown survival benefits associated with use of adjuvant chemotherapy in early-stage breast cancer. The optimal time to initiation of adjuvant chemotherapy and impact according to breast cancer subtype, however, are less clear.

In the current study, Mariana Chavez-MacGregor and colleagues, from MD Anderson Cancer Center, retrospectively reviewed the medical records of 6,827 women with stage I to III invasive primary breast cancer who received adjuvant chemotherapy between 1997 and 2011. Patients were categorised according to time from definitive surgery to adjuvant chemotherapy into one of three groups: <30 days, 31 to 60 days and >60 days.

Results show that for patients with HER2-positive tumours who received trastuzumab, the five-year overall survival (OS) estimate was 88% for those starting chemotherapy within 30 days, versus 87% for those starting chemotherapy within 31 to 60 days, and 75% for those starting chemotherapy after 60 days ($P$=0.01).

Patients with triple-negative breast cancer had a 74% decrease in overall survival if they started chemotherapy between 31 and 60 days of surgery compared with starting within 30 days (HR 1.74, 95% CI 1.32–2.29, $P$<0.001).

The subgroup of patients with stage III disease had a 76% decrease in overall survival if they started chemotherapy more than 60 days after surgery versus 30 days or less (HR 1.76, 95%CI 1.26–2.46, $P$<0.001). Among patients with stage II disease, the distant-relapse-free survival (DRFS) decreased by 20% if they started chemotherapy more than 60 days after surgery versus 30 days or less (HR 1.20, 95% CI 1.02–1.43, $P$=0.03).

The timing of chemotherapy showed no effect on outcomes (OS, RFS, or DRFS) in patients with stage I disease, HER2-positive tumours not treated with trastuzumab, and hormone-receptor-positive tumours.

"Among patients with stage II and III BC [breast cancer], TNBC [triple-negative BC], and HER2-positive tumors, every effort should be made to avoid postponing the initiation of adjuvant chemotherapy," write the authors. Since adverse outcomes occurred when chemotherapy was delayed by more than 60 days, they add, medical oncologists should have sufficient time to initiate treatment.

In an accompanying commentary, Marco Colleoni, from the European Institute of Oncology, Milan, and Richard Gelber, from the Dana-Farber Cancer Institute, Boston, write: "A review of the cause of death for these patients may reveal that co morbidities (e.g., cardiac) delaying initiation of anthracycline-containing chemotherapy may be exacerbated by trastuzumab, and that the results shown... are not entirely related to delayed administration of chemotherapy." Since two-thirds of the patients had hormone-receptor-positive disease, they add, there is no indication that time to initiation of chemotherapy makes much difference for the majority of patients.

■ D de Melo Gagliato, A Gonxalex-Angulo, X Lei et al. Clinical impact of delaying initiation of adjuvant chemotherapy in patients with breast cancer. *JCO* 10 March 2014, 32:735–744

■ M Colleoni, R Gelber. Time to initiation of adjuvant chemotherapy for early breast cancer and outcome: the earlier, the better? [editorial] *ibid* pp 717–719

### Young families a barrier to radiotherapy for breast cancer

■ JNCI

Competing demands of childcare create barriers for women completing radiation therapy after breast cancer surgery. A US study has found that having at least one child aged less than seven years old resulted in statistically significant lower odds of receiving radiotherapy than having no children or older children.

Evidence-based literature has confirmed the effectiveness of radiotherapy after breast-conserving surgery, especially among young patients. While several population-based studies have investigated factors associated

with radiotherapy compliance, the majority have focused on elderly populations. Estimates suggest that approximately 60% of breast cancer patients diagnosed between 2005 and 2009 were aged less than 65 years.

The current study by Ya-Chen Tina Shih and colleagues, from the University of Chicago, explored factors associated with non-compliance with radiotherapy among insured young patients (aged 20–64 years). The investigators used a nationwide database to review medical and prescription records of 21,008 patients with insurance coverage who received breast cancer surgery between January 2004 and December 2009.

Results showed that 892 women (4.25%) had at least one child under seven years old; 1,584 (7.54%) had all children older than six years and at least one aged 7–12 years; 2,016 (9.6%) had all children older than 12 and at least one child aged 13–17 years; and 16,516 (78.62%) had no children or all children aged older than 18.

In comparison with women with one child under 7, those with at least one child aged 7– 12 were 32% more likely to receive radiotherapy (OR 1.32, 95%CI 1.05–1.66, *P*=0.02); those with one child aged 13–17 were 41% more likely to receive radiotherapy (OR 1.41, 95%CI 1.13–1.75, *P*=0.002); and those with no children or children older than 18 were 38 % more likely to receive radiotherapy (OR=1.38, 95%CI 1.13–1.68, *P*=0.001).

Statistically significant lower odds of receiving radiotherapy were observed among patients enrolled in a Health Maintenance Organization (HMO) or Preferred Provider Organization (PPO) with capitation versus other plan types (OR 0.70, 95% CI 0.63–0.77), and for patients who travelled long distances for radiotherapy treatment, determined by evaluating whether the patient's geographical area differed from her healthcare provider (OR = 0.72; 95%CI 0.60–0.86). In addition, results show that patients who are the primary holders of insurance policies are more likely to have radiotherapy (OR = 1.20; 95%CI 1.10–1.31).

"Our finding that a young child in the home is a barrier to completion of appropriate breast cancer therapy underscores the unique challenges confronted by younger (aged 20–50 years) cancer patients," write the authors. Additional work, they add, is needed to understand the impact of family structure on other aspects of cancer care and to develop robust interventions tailored to the unique needs of younger cancer patients.

■ I-W Pan, BD Smith, Y-CT Shih. Factors contributing to underuse of radiation among younger women with breast cancer. *JNCI*, published online 7 December 2013, doi:10.1093/jnci/djt340

## Survey finds hours of care related to burnout

■ Journal of Clinical Oncology

Hours per week devoted to patient care is the dominant professional factor associated with oncologist 'burnout', a survey by the American Society of Clinical Oncology (ASCO) has found. The survey, which is the first national study to evaluate burnout and career satisfaction among US oncologists since 2003, reports that 45% of oncologists have at least one symptom of burnout and that oncologists in academic practice display greater job satisfaction than those in private practice.

The very fact that oncologists work long hours, and are continually exposed to death and suffering, places them at risk of burnout, a syndrome characterised by emotional exhaustion, treating people as if they are objects, and loss of meaning or purpose in work. Studies suggest that physicians experiencing burnout are more likely to reduce their work hours and/or pursue early retirement.

Between October 2012 and March 2013, Tait Shanafelt and colleagues, supported by ASCO, undertook a survey evaluating the personal and professional characteristics associated with career satisfaction and burnout among US oncologists. Altogether 2,998 US oncologists were contacted, of whom 1,117 (37.3% of overall sample) completed full-length surveys. Of these, 377 (33.8%) worked in academic practice, and 482 (43.2%) in private practice, with the remainder working in other settings. The full-length survey included 60 questions exploring a variety of personal and professional characteristics, with burnout measured using the Maslach Burnout Inventory (MBI) – a 22-item questionnaire.

Overall results showed that 484 oncologists (44.7%) were burned out on the emotional exhaustion and/or depersonalisation domain of the Maslach Burnout Inventory, with 45.9% of oncologists in academic practice displaying burnout versus 50.5% of those in private practice (*P*=0.18). In a multivariable analysis, younger age and greater number of hours spent seeing patients each week were independently associated with burnout for oncologists in both practice settings. Each additional year of age reduced the risk of burnout by approximately 4–5%, and each additional hour spent seeing patients increased the risk of burnout by 2–4%.

Differences between oncologists working in the different settings included that oncologists in academic practice were more likely to focus on treating patients with one particular type of cancer, spent a greater proportion of their time supervising physicians in training, and saw nearly half as many patients in outpatients per week as those in private practice (37. 4 vs 74.2; *P*<0.001).

Overall a higher percentage of respondents working in academic practice than private practice said they would become a physician again (87.5% vs 79.2%, *P*=0.0016) and the same was true about becoming an oncologist again (85.1% vs 77.5%, *P*=0.0053).

"The strong, incremental relationship between time devoted to patient care and burnout is concerning, especially given the projected shortage in the supply of oncologists during the coming decades," write the authors. Given the prevalence of burnout and evidence that it erodes physician personal

health and quality of care, they add, future studies need to focus on how to address this problem.

■ TD Shanafelt, WJ Gradishar, M Kosty et al. Burnout and career satisfaction among US oncologists. *JCO* 1 March 2014, 32:678–686

## Head and neck cancer: nurse-led interventions improve quality of life

■ British Journal of Cancer

Nurse counselling and after therapy intervention (NUCAI) improved health-related quality of life and depressive symptoms among patients with head and neck cancer, a Dutch longitudinal randomised controlled trial has found.

Patients with head and neck cancers are prone to have poor health-related quality of life (HRQoL) following treatment, with people known to experience deterioration of HRQoL directly after starting treatment and up to 11 years after completion. The multidimensional problems observed include issues with emotional and physical function, general cancer symptoms (e.g. fatigue and pain) and symptoms specific to head and neck cancers (e.g. swallowing and dry mouth). Nurses, who are already involved with patient care, and have skills and knowledge around medical and practical aspects of head and neck cancer, are considered to be in a key position to deliver interventions.

Between January 2005 and September 2007, Ingeborg van der Meulen and colleagues, from the University Medical Centre Utrecht, the Netherlands, randomly allocated 205 patients with head and neck cancer from outpatient oral maxillofacial and otorhinolaryngology clinics to NUCAI ($n$=103) or usual care ($n$=102). The NUCAI intervention, provided by trained nurses, aimed to help patients manage the physical, psychological and social consequences of their disease and its treatment with advice, emotional support, education and behavioural training.

Nurses opened sessions with discussions of current physical problems and explored life domains including home situations, (resuming) work, household and leisure activities, mood and emotional distress, partner relations and intimacy and family and social life. Patients could be referred to psychiatrists or health professionals specialising in psychosocial problems.

Patients received a maximum of six counselling sessions lasting 45 to 60 minutes every two months, over a period of one year, starting six weeks after completion of cancer treatment. Health-related quality of life was evaluated with the EORTC QLQ-C30 and QLQ H&N35, while depressive symptoms were evaluated with the CES-D.

Results show that at 12 months the intervention group showed a significant improvement in emotional and physical functioning, including pain, swallowing, social contact, mouth opening and depressive symptoms ($P$<0.05). At 18 months, global quality of life, role and emotional functioning, pain, swallowing, mouth opening and depressive symptoms were significantly better among patients in the intervention group than in the control group, and at 24 months emotional functioning and fatigue were significantly better in the intervention group.

The programme, believe the authors, appears a promising intervention for implementation in daily clinical practice. "Compared with other, more intensive, interventions... we consider the NUCAI to be a relatively low-cost intervention, given its nurse-led approach and the relatively few sessions involved. Moreover, findings suggest that it can be implemented in the follow-up care for HNC [head and neck cancer] patients, although the overall costs and feasibility of the intervention remain to be investigated," write the authors.

It is important, they add, that nurses who offer the intervention have extensive experience in the care of patients with head and neck cancer and good communication skills, and are self-reliant and able to work closely with other professionals.

■ IC van der Meulen, AM May, JRJ de Leeuw et al. Long-term effect of a nurse-led psychosocial intervention on health-related quality of life in patients with head and neck cancer: a randomised controlled trial. *BJC* 4 February 2014, 110:593–601

## Complications of prostate cancer treatment defined

■ Lancet Oncology

Patients with prostate cancer undergoing primary radiotherapy have higher incidences of hospital admissions, rectal or anal procedures, open surgical procedures and secondary malignancies than patients undergoing surgery, a population-based retrospective cohort study has found. Conversely, the Canadian investigators showed that patients who had primary surgery were more likely to undergo subsequent urological procedures.

Studies of complications resulting from surgery or radiotherapy for prostate cancer have focused largely on symptoms of incontinence and erectile dysfunction. In the current study, Robert Nam and colleagues, from Sunnybrook Health Sciences Centre, Toronto, set out to assess other complications associated with prostate cancer treatments.

The team used administrative hospital data, physician billing codes, and cancer registry data to analyse a cohort of 32,465 men in Ontario who underwent either radical prostatectomy ($n$=15,870) or radiotherapy alone ($n$=16,595) to treat prostate cancer, between 2002 and 2009. They measured the five-year cumulative incidence of key treatment-related complication endpoints: hospital admissions, urological, rectal, or anal procedures, open surgical procedures and secondary malignan-

cies. To assess the baseline incidence of these outcomes in the general population, the team randomly identified 32,465 age-matched controls with no history of prostate cancer.

Results showed that patients given radiotherapy had a higher incidence of complications for hospital admissions, rectal or anal procedures, open surgical procedures, and secondary malignancies at five years than did those who underwent surgery (adjusted hazard ratios ranged from 2.08 to 10.8, *P*<0.0001). The cumulative incidence in years 5 to 9 of developing a second malignancy was 4.5% (95%CI 3.8–5.5) in the radiotherapy group versus 1.8% (95%CI 1.3–2.4) in the surgery group.

The most common site of second malignancies was the gastrointestinal tract (87 per 100,000 person-years in the radiotherapy group and 28 per 100,000 person-years in the surgery group; *P*<0·0001).

The number of urological procedures, however, was lower in the radiotherapy group than in the surgical group (adjusted HR 0.66, 95%CI 0·63–0·69; *P*<0·0001). All risks were significantly higher for prostate cancer patients than the 32,465 matched controls with no history of prostate cancer.

"Clinicians should discuss these complications, in addition to the well-known adverse effects of incontinence and erectile dysfunction, with their patients when talking about treatment options for clinically localised prostate cancer," write the authors.

In an accompanying commentary, Michael J Eble from RWTH Aachen University, Germany, writes that, while population-based studies have the advantage of delivering sufficient patient numbers to identify small increases in the risk of secondary malignancies, the effects can be "negated by the presence of unbalanced confounders".

■ R Nam, P Cheung, S Herschom et al. Incidence of complications other than urinary incontinence or erectile dysfunction after radical prostatectomy or radiotherapy for prostate cancer: a population-based cohort study. *Lancet Oncol* February 2014, 15:223–231

■ MT Eble. Complications from treatment of localised prostate cancer. *ibid* pp134–135

## Sentinel node biopsy: patients with intermediate thickness melanomas benefit most

■ New England Journal of Medicine

Sentinel node biopsy prolongs distant disease-free survival and melanoma-specific survival in patients with lymph node metastasis from primary tumours of intermediate thickness, the final ten-year analysis of the Multicenter Selective Lymphadenectomy Trial (MSLT-I) has concluded.

The MSLT-I trial, initiated in 1994, set out to investigate whether sentinel-node biopsy with immediate lymphadenectomy of involved nodes yielded better outcomes in melanoma than 'watchful waiting' with delayed lymphadenectomy, performed only when nodal recurrence becomes evident during observation. Sentinel-node biopsy was developed by Donald Morton, the first author of the current study, who died just before publication. The five-year results of the third interim analysis, published in 2006, focused on patients with intermediate thickness primary tumours, while the current ten-year follow-up data also includes patients with thick primary melanomas.

The final report involved 1,560 patients with localised cutaneous primary melanomas who were randomly assigned to undergo sentinel-node biopsy plus immediate lymphadenectomy if metastases were detected in sentinel nodes (*n*=943) or close observation with delayed lymphadenectomy if nodal metastases developed during observation (*n*=617). Altogether 1,270 patients had intermediate thickness lesions (1.20–3.50 mm) and 290 patients had thick lesions (>3.50 mm).

Among subjects with intermediate thickness melanomas, ten-year disease-free survival was 71.3% for patients in the biopsy group versus 64.7% for those in the observation group (HR for recurrence or metastasis = 0.76; *P*=0.01). For subjects with thick melanomas, ten-year disease-free survival was 50.7% for patients in the biopsy group versus 40.5% for those in the observation group (HR 0.70; *P*=0.03).

For patients with intermediate-thickness melanomas and nodal metastases, biopsy-based management improved ten-year distant-disease-free survival (HR distant metastasis 0.62; *P*=0.02) and ten-year melanoma-specific survival (HR for death from melanoma = 0.56; *P*=0.006). This was not seen in patients with thick melanomas. For the overall study population (where only one in five subjects had nodal metastases) treatment-related differences were not found for ten-year melanoma-specific survival.

"Although some patients with nodal metastases from thick melanomas may benefit from lymphadenectomy, our findings suggest that the timing of that intervention is not as critical as it is for patients with intermediate-thickness melanomas," write the authors, adding that the number of patients in the trial with thin melanomas was too small to draw conclusions.

In an accompanying commentary, Charles Balch from the University of Texas Southwestern Medical Center, Dallas, and Jeffrey Gershenwald from MD Anderson Cancer Center, Houston, write: "This practice changing trial shows the important role of early identification and surgical removal of regional metastases, both in obtaining staging information and in improving survival in defined cohorts of patients with melanoma."

■ DL Morton, JF Thompson, AJ Cochran. Final trial report of sentinel-node biopsy versus nodal observation in melanoma. *NEJM* 13 February 2014, 370:599–609

■ CM Balch, JE Gershenwald. Clinical value of the sentinel-node biopsy in primary cutaneous melanoma. *ibid* pp663–664