Scandinavians show better awareness of age-related cancer risks

NEWS ROUND

Large international differences exist in the extent to which people are aware that cancer risks increase with age according to the first study ever to examine differences in cancer awareness and beliefs between high-income countries. Symptom recognition appears more uniform, however.

International comparisons have shown wide differences in cancer survival between high-income countries with good cancer registration systems and good access to health care. For cancers of the lung, breast, bowel and ovary diagnosed between 1995 and 2007, the International Cancer Benchmarking Partnership (ICBP) found that Australia, Canada and Sweden had the highest survival, Norway had an intermediate rate, and Denmark and the UK had the lowest rates.

In the current study, Lindsay Forbes and colleagues, from King’s College, London, set out to examine differences in cancer awareness and beliefs across ICBP study countries and to explore how these might contribute to patterns of survival. Between May and September 2011, investigators carried out a population-based telephone survey of 19,079 men and women aged 50 years or more in Australia, Canada, Denmark, Norway, Sweden and the UK. The survey measured cancer awareness and beliefs using the newly developed Awareness and Beliefs about Cancer (ABC) measure.

Results show that the mean number of symptoms recognised (out of 11) were 8.22 for the UK, 8.35 for Denmark, 8.49 for Norway, 7.71 for Sweden, 8.34 for Australia and 8.70 for Canada. Awareness that cancer risks increase with age was 14% in the UK, 13% in Canada, 16% in Australia, 25% in Denmark, 29% in Norway and 38% in Sweden.

In the UK, 14.5% of respondents said embarrassment put them off going to the doctor with symptoms that might be serious, compared to 5.8% in Denmark, 9.4% in Norway, 9.2% in Sweden, 11.6% in Australia and 9.6% in Canada. Additionally, 34.3% of respondents in the UK said they would be worried about wasting their doctor’s time compared to 11.7% in Denmark, 10.9% in Norway, 9.3% in Sweden, 14.2% in Australia and 21.1% in Canada. In the UK, 27.5% were concerned about what the doctor might find, versus 23.9% in Denmark, 19.8% in Norway, 23.1% in Sweden, 22% in Australia and 25.4% in Canada.

“The pattern of differences in cancer awareness and beliefs between the participating countries did not follow the pattern of differences in survival, but there was some evidence that it followed cultural/language demarcations: Scandinavian people had lower levels of barriers to symptomatic presentation and better awareness of age related risk than people in the Commonwealth countries,” write the authors.

The findings, they add, have specific implications for individual countries. In Denmark, poor cancer survival rates are unlikely to be due to poor cancer awareness; while in the UK interventions to promote early presentation might usefully focus on addressing awareness of age-related risks and increasing people’s confidence about approaching GPs with possible cancer symptoms.


Bioradiotherapy does not benefit larynx preservation

In patients with cancer of the larynx there is no evidence that bioradiotherapy with cetuximab delivers benefits over chemoradiotherapy with cisplatin for larynx preservation, the phase II TREMPLIN study has found.

To date, two main approaches have been evaluated for larynx preservation: induction chemotherapy followed by radiotherapy in good responders, and concurrent chemotherapy and radiotherapy. In Europe induction chemotherapy based protocols have tended to be preferred; while in the US concurrent chemotherapy and radiotherapy has been regarded as the best approach for avoiding total laryngectomy. For each approach pros and cons have been identified: with induction chemotherapy only good responders have a chance of avoiding surgery, while with the concurrent approach all patients avoid surgery, but treatment is
associated with acute and late toxicities. In a recent randomised trial, bioradiotherapy with cetuximab delivered improvements in overall survival in comparison to radiotherapy alone, suggesting bioradiotherapy might offer an alternative to chemoradiotherapy.

The French Groupe Oncologie Radiothérapie Tête et Cou set out to compare the efficacy and safety of induction chemotherapy followed by chemoradiotherapy or bioradiotherapy for larynx preservation. Between March 2006 and April 2008, 153 previously untreated patients with stage III to IV larynx/hypopharynx squamous cell carcinoma, from 20 centres, received three cycles of induction chemotherapy (docetaxel and cisplatin on day 1 and fluorouracil on days 1 through 5). All 116 patients who responded (i.e. who achieved >50% response rate) received conventional external beam radiotherapy and were then randomly allocated to the cisplatin arm (chemoradiotherapy, n=60) or the cetuximab arm (bioradiotherapy, n=56). Patients achieving less than 50% response rates were not eligible for random assignment, and underwent immediate salvage total laryngectomy.

Results showed there were no significant differences between the two groups for the primary and secondary endpoints. At three months, larynx preservation was achieved in 95% of patients in the cisplatin arm versus 93% in the cetuximab arm. At 18 months, larynx function preservation was achieved in 87% in the cisplatin group versus 82% in the cetuximab group, and overall survival was 92% for the cisplatin group versus 89% for the cetuximab group. For both toxicity was high, while treatment compliance was higher in patients receiving cetuximab than cisplatin.

“There is no evidence that one treatment was superior to the other or could improve the outcome reported with induction chemotherapy followed by radiotherapy alone,” conclude the authors.

In an accompanying commentary, Everett Vokes, from the University of Chicago Medical Center, Illinois, writes, “We cannot conclude that cisplatin-radiotherapy and cetuximab-radiotherapy are equivalent because the favorable survival observed in both arms was likely a function of TPF (docetaxel, cisplatin, fluorouracil) induction and subsequent patient selection and not as a result of the intensification of radiotherapy.” The major challenge for organ preserving protocols, he adds, is not to increase already good outcomes of responders, but to improve outcomes for non-responders, which will not be achieved by excluding them from randomisation. “The TREMPLIN trial... reminds us that, when designing clinical trials, we must prioritize the specific deficiencies of current standard approaches that we need to address,” writes Vokes.

Wide variation in lung cancer survival

Thorax

While differences in stage at diagnosis explain some international variations in lung cancer survival, wide disparities in stage-specific survival suggest factors such as treatment also play an important role, a population-based study in nearly 60,000 patients has found.

Stage at diagnosis has often been suggested as one of the primary explanations for lung cancer survival being low in certain countries (such as the UK), on the grounds that patients go to see their doctors too late for treatment to be effective. Understanding why these survival differences occur is considered helpful, since it would facilitate policy changes to bring survival up to the highest international standards.

In the current study, Sarah Walters and colleagues, from the London School of Hygiene and Tropical Medicine, obtained population-based data that had been routinely collected on 57,352 patients, aged between 15 and 99 years, diagnosed with lung cancer between 2004 and 2007, whose details had been recorded in national cancer registries in Australia, Canada, Denmark, Norway, Sweden and the UK. The authors then monitored patients to estimate survival at one year and 18 months after diagnosis, for each diagnostic stage, for both non-small-cell lung cancer (NSCLC) and small-cell lung cancer (SCLC).

Results showed that, after adjustment for differences in age and death from other causes, one-year survival rates after a diagnosis of lung cancer were 46% in Sweden, 42% in Australia, 42% in Canada, 39% in Norway, 34% in Denmark, and 30% in the UK. Taking the example of patients diagnosed at stage IV for NSCLC, one-year survival rates were 16.8% in Canada, 21.4% in Denmark, 25.9% in Sweden and 15.5% in the UK. Taking the example of SCLC, the one-year survival rates for patients with a diagnosis at stage IV were 18.3% in Canada, 23% in Denmark, 26.8% in Sweden and 14.4% in the UK.

“International differences in survival were also evident within each stage of disease for both types of lung cancer: generally low in the UK and high in Sweden,” write the authors.

Differences in the thoroughness of staging, they suggest, may have contributed to international variation in stage distributions and stage-specific survival, with the proportion of histologically verified tumours ranging from 74% in the UK to 94.8% in Sweden. In the UK, report the authors, elderly patients have been less likely to undergo invasive procedures due to concerns about frailty.

“Low stage-specific survival in the UK could conceivably arise in part because of suboptimal staging, and this misclassification of stage in a proportion of patients could lead to inappropriate treatment and therefore overall lower survival,” they write.

In order to understand the impact of different staging procedures on international...
Long-term functional outcomes: no difference between prostatectomy and radiotherapy

At 15 years’ follow up, no significant differences in functional outcomes for urinary incontinence, erectile dysfunction and bowel urgency were found between men treated for early prostate cancer with surgery and those treated with external beam radiotherapy. These findings contrast with earlier two- and five-year data from the same study, showing advantages in urinary incontinence and erectile function for patients undergoing radiotherapy, and advantages in bowel urgency for patients undergoing prostatectomy. Regardless of treatment, the study shows the risk of suffering functional decline at 15 years is considerable.

As the median life expectancy after treatment for prostate cancer is 13.8 years, a long-term analysis to understand outcomes for men choosing between radiotherapy and surgery is considered important. The literature, however, largely reports short-term (1–3 years) or intermediate term (4–5 years) outcomes, which may not reflect the long-term experience of men undergoing prostate cancer treatment.

In the current study, to assess the long-term effects of localised prostate cancer treatment, David Penson and colleagues, from Vanderbilt University Medical Center in Nashville, Tennessee, analysed the Prostate Cancer Outcomes Study (PCOS), which followed 3533 men with prostate cancer diagnosed in 1994 and 1995, who underwent either surgery or definitive radiation therapy within a year of diagnosis. The final analysis included 1655 men aged between 55 and 74 when diagnosed with localised prostate cancer, of whom 1164 underwent surgery and 491 underwent radiotherapy. Functional status was assessed at baseline and 2, 5 and 15 years after diagnosis.

Results show that 15 years after diagnosis, 322 of the men who underwent prostatectomy (27.7%) and 247 of the men who underwent radiation therapy (50.3%) had died.

At two years, patients undergoing prostatectomy were more likely to have urinary incontinence than those undergoing radiotherapy (OR 6.22), at five years they were still more likely to have urinary incontinence (OR 5.10), but at 15 years no significant difference could be found between the two groups.

At two years, patients undergoing prostatectomy were more likely to have erectile dysfunction than those undergoing radiotherapy (OR 3.46), at five years they were still more likely to have erectile dysfunction (OR 1.96), but at 15 years no significant difference was found between the two groups.

At two years, men in the prostatectomy group reported significantly lower rates of bowel urgency than those in the radiotherapy group (OR 0.39), at five years they were still less likely to have bowel urgency, but at 15 years there was no significant difference (OR 0.98).

“Men undergoing prostatectomy or radiotherapy for localized prostate cancer had declines in all functional outcomes throughout early, intermediate, and long-term follow-up.

“Whereas short- and intermediate-term data reveal differences in functional profiles among men undergoing prostatectomy and radiotherapy, at 15 years we observed no significant relative between-group differences,” conclude the authors.

Given the absence of an untreated age-matched control cohort, they acknowledge that the precise contribution of prostate cancer treatment to age-dependent changes in urinary, sexual, and bowel function remains unknown.

MEK inhibitors renew efficacy of radioiodine

Administration of selumetinib delivers clinically meaningful increases in iodine uptake and retention for patients with thyroid cancer refractory to radioiodine, a pilot clinical study funded by the American Thyroid Association has concluded.

While radioiodine (iodine-131) remains the mainstay of therapy for patients with metastatic thyroid cancer of follicular origin, many patients have tumours unable to concentrate iodine, resulting in radioiodine resistance. The result is a poor prognosis, with 10-year survival rates of around 10% among this group of patients, versus approximately 60% among patients with metastatic thyroid cancers that retain iodine.

Approximately 70% of papillary thyroid cancers have gene mutations encoding the growth factor receptors RET or NTRK1, and the three isoforms of RAS and BRAF. Activation of these proteins stimulates mitogen-activated protein kinase (MAPK) signalling, which inhibits the expression of thyroid hormone biosynthesis genes, thereby facilitating iodine uptake in organs.

James Fagin and colleagues, from the Memorial Sloan Kettering Cancer Center in New York, set out to determine whether selumetinib, which inhibits the MEK1 and MEK subtypes of MAPK kinase, might reverse refraction to radioiodine.
For the study, performed between August 2010 and December 2011, after stimulation with thyrotropin alfa, 24 patients with differentiated thyroid carcinoma of follicular cell origin who met criteria for radioiodine refractory disease, underwent dosimetry with iodine-124 PET both before and four weeks after treatment with selumetinib (75 mg twice daily).

Of the 20 patients evaluated (two of the original 24 had baseline QT levels outside the study range and two dropped out), 12 had iodine-124 uptake that was new, increased, or both after selumetinib. In eight of these, the second iodine-124 PET study indicated that the absorbed radiation dose in the lesion would equal or exceed 2000 cGy with 300 mCi of radioiodine or less; these patients continued to receive selumetinib, and they received therapeutic radioiodine. It is noteworthy that the 12 patients included four out of nine patients with BRAF mutations and five out of five patients with NRAS mutations. However, while all five patients with NRAS-mutant tumours exceeded the dosimetry threshold for receiving therapeutic radioiodine with selumetinib, this was the case for only one of the patients with BRAF mutations.

Of the eight patients treated with radioiodine, five had confirmed partial responses and three had stable disease; and all patients showed decreases in serum thyroglobulin level, with a mean reduction of 89%. No toxic effects of grade 3 or higher attributable to selumetinib were observed, add the authors. One patient, who was treated with 139 mCi of radioiodine during the study, received a diagnosis of myelo dysplastic syndrome more than 51 weeks after radioiodine treatment, with progression to acute leukaemia.

“These results provide a proof of principle that MEK inhibitors can induce iodine uptake and retention in thyroid tumours. An advantage of this therapeutic strategy over long-term treatment with small-molecule kinase inhibitors alone is that only a short course of drug therapy is required to elicit a durable clinical effect,” write the authors.

Enhanced iodine uptake, they add, was also observed in bone and nodal metastases, both of which have been found to be comparatively refractory to treatment with kinase inhibitors.

- A Ho, R Greval, R Leboeuf et al. Selumetinib enhanced radioiodine uptake in advanced thyroid cancer. NEJM 14 February 2013, 368:623–632

Study questions value of tumour boards

The presence or absence of tumour boards in a large integrated health system does not influence service quality or survival “in any meaningful way”, a study in the US Veterans Affairs (VA) health system has found.

Tumour boards involve the discussion of newly diagnosed cancer patients by multidisciplinary teams involving medical, surgical and radiation oncologists, in addition to pathologists, diagnostic imaging specialists, palliative care doctors, and social workers. Tumour boards are perceived to be so important that the American College of Surgeons’ Commission on Cancer Program Accreditation requires cancer programs to have multidisciplinary cancer conferences to prospectively review cases. Despite widespread use, no data exist on the benefits of tumour boards for cancer care.

In the current study, Nancy Keating and colleagues, from Harvard Medical School, in Boston, Massachusetts, assessed whether the presence of a tumour board (either general or site-specific) was associated with recommended care and with survival outcomes. Information gathered from 138 VA medical centres was linked to cancer registry and administrative data to gauge the receipt of stage-specific recommended care and survival in patients with colo rectal, lung, prostate, haematologic, and breast cancers. Patients were diagnosed between 2001 and 2004, and followed through to 2005.

The results showed that 103 (75%) of the 138 hospitals surveyed had at least one tumour board, 62 centres had a single tumour board that discussed cases from multiple cancer sites, and 41 had more than one disease-specific tumour board. The presence of a tumour board was associated with only seven of 27 measures assessed (all P<0.005). When researchers applied a Bonferroni correction (a method used when several dependent or independent statistical tests are performed simultaneously), only one measure was associated with tumour boards. The measure was that patients with limited-stage small-cell lung cancer reviewed by tumour boards were statistically more likely to undergo chemotherapy or radiation than those not reviewed (P=0.00185).

The authors comment that the lack of association of multidisciplinary tumour boards with measures of use, quality or survival could mean that tumour boards do not influence the quality of cancer care. “It might also mean that tumor boards are only as good as their structural and functional components and the expertise of the participants, and because tumor boards likely vary in their efficacy depending on these factors, measuring only the presence of a tumor board may not be sufficient to understand their effects,” write the authors. Additional research, they add, is needed to understand the structure and format of tumour boards leading to the highest quality care.

In an accompanying commentary, Douglas Blayney, from Stanford University School of Medicine in California, writes that there should be no surprise that improved performance on the process or outcome measures of quality is not predicted by the existence of team meetings. “Anyone who has ever played a team sport, worked with a laboratory team, led a clinical trial team, or led a patient care team soon realizes that huddles, lab meetings, cooperative group meetings, or attending physician rounds don’t get the job done.”

- D Blayney. Tumor boards (team huddles) aren’t enough to reach the goal. ibid pp 82–84