Cancer in old age—is it inadequately investigated and treated?

N J Turner, R A Haward, G P Mulley, P J Selby

The proportion of the United Kingdom population over 75 years of age will increase from around 7% to nearly 11% in the next 50 years, with a disproportionate rise in those over 85 years. There will be a large increase in the number of elderly patients with cancer. Already over one third of cancers are diagnosed in people over 75, yet we do not know how best to investigate and treat cancers in these patients. Many clinical trials have used arbitrary upper age limits. Even trials in allegedly elderly subjects start at age 65. Very few studies include large numbers of old (over 75) or very old (over 85) people.[1] The role and effectiveness of many cancer treatments is therefore not evidence based in those most affected.

Studies of cancer care in elderly patients show fewer diagnostic and staging procedures and less treatment with advancing age. Disease specific survival rates decline with age.[2–6] This is illustrated by data from the Yorkshire Cancer Registry on histological confirmation (a useful marker for the adequacy of investigation), receipt of definitive treatment, and relative survival in relation to age group (table).[7] The Yorkshire Cancer Registry is one of the registries used in the Eurocare study. It covers a population of 3.7 million, constituting 7.2% of the total population of England and Wales.

Why do elderly people seem to be underinvestigated and undertreated? Perhaps the age associated decline in functional reserve and the increase in comorbid conditions discourage aggressive interventions. Do elderly patients refuse to have certain treatments? Do their relatives dissuade them from having therapy? Is there ageism among doctors and other health professionals? Do non-specialists protect frail older patients from what they perceive to be "unnecessary" procedures and treatments? We decided to review published reports on the investigation and treatment of cancer in old age to try to answer some of these questions.

Summary points

- Although more than a third of cancers are diagnosed in people over 75, this group is less extensively investigated and receives less treatment than younger patients
- 75 year old women and 75 year old men have life expectancies of 11.1 years and 8.5 years respectively
- Reduced levels of intervention are not wholly explained by appropriate adjustment for comorbidity or frailty
- Some elderly people can tolerate chemotherapy, surgery, and radiotherapy just as well as younger patients, and regimens and protocols can be modified in less fit patients
- Ageism in healthcare staff, lack of awareness of life expectancy and treatments available, and beliefs and fears about cancer and its treatment in elderly patients and their relatives may be factors in this disparity

Methods

We performed a Medline search from 1980 to 1998, using the terms "cancer," "elderly," and "old age." We also scrutinised bibliographies of the articles obtained from the search for additional references. Papers selected included recent review articles and trials specifically in elderly people.

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Proportion (%) of cancers confirmed by histology, cancer patients with no definitive treatment, and cancer patients surviving five years, by age group, Yorkshire 1989-93

	Confirmed by histology			No definitive treatment			Five year survival*		
Site	0-64	65-74	75+	0-64	65-74	75+	0-64	65-74	75+
Breast	97	91	63	1	4	11	71	68	54
Colon	95	89	75	9	16	31	43	39	37
Lung	80	70	44	32	48	76	8	5	2
Prostate	94	91	78	6	8	15	46	46	42
Skin (non-melanoma)	98	98	96	1	1	2	98	99	100
Stomach	90	86	70	32	44	66	16	11	9

*Excludes deaths from other causes.

Comorbidity

Some researchers have tried to correct for comorbidity. One study has shown that the apparent age bias is explained by excess comorbidity in elderly subjects.[6] However, others show that age is an independent negative predictor of getting definitive treatment.[3] After correcting for comorbidity, one group found that the age bias remained for treatments received, but not for diagnostic investigations.[4] There is no validated scale for measuring comorbidity, so comparison between studies is difficult. Scales of performance status, function, and quality of life are well validated, but practice in the disciplines of oncology and care of the elderly has led to different things being measured. The former has tended to focus on pathology and impairment, and the latter has focused on disability and handicap. However, both specialties are beginning to use health related quality of life measures.

Reduced function

The word "frail" is often used to describe elderly patients, but it needs a clear definition. Recent efforts at achieving this address four measurable components of reduced function: musculoskeletal function, aerobic capacity, cognitive and integrative neurological function, and nutritional state. Frailty is defined as a multisystem reduction in physiological capacity which renders the old person vulnerable to relatively small environmental challenges.[8] While this provides a useful, potentially measurable concept, no validated scale for frailty exists for general use.

Treatment

Chemotherapy

Surprisingly little is clear about the place of chemotherapy in elderly patients. Studies have included patients with controlled comorbidity (for example, hypertension, coronary artery disease, and diabetes mellitus), with no adverse effect on outcome. Known side effects of some chemotherapeutic drugs (such as the cardiotoxicity of anthracycline drugs) might lead doctors sensibly to restrict their use in patients with pre-existing cardiological problems. However, though cardiovascular diseases are said to predispose to the cardiotoxicity of these drugs, this is not certain.[9]

Aspects of healthy ageing such as the age related decline in the glomerular filtration rate can increase the toxicities of some drugs. Reducing the dosage in relation to the creatinine clearance rate can compensate for this, as can the use of less nephrotoxic drugs (such as carboplatin instead of cisplatin). Survival in elderly patients treated with reduced doses is sometimes comparable to that of younger patients treated with full dose protocols. Whether the incidence of toxic side effects increases with age is more controversial.[9] Myelosuppression may be greater in older people, but the use of haemopoietic growth factors such as granulocyte colony stimulating factor can help to overcome this.[10] Elderly patients tolerate some chemotherapy regimens, even at full dose, just as well as their younger counterparts do, but some authors caution against the use of intensive regimens.[11] Treatment protocols have been designed for patients who are unsuitable for standard regimens because of comorbid conditions.[12]

Surgery

Surgery is performed less often in elderly patients with non-small cell lung cancer, despite the tumour being operable.[4] This surgery can be performed safely in elderly patients selected according to the same anatomical and physiological criteria used in younger subjects.[13] Operative risk increases with age, but with modern anaesthetic and surgical techniques this can be reduced to acceptable levels, even in the oldest age groups.[14] Attention to good preoperative and postoperative care is of particular importance in elderly patients with comorbidity.

Colonic cancer surgery is performed on most patients, regardless of age,[4] and this is sometimes a palliative rather than a curative procedure. Elderly women with ovarian cancer, in whom optimal "debulking" of the tumour offers improved survival, are much less likely to have surgery.[5] In breast cancer, too, reduced use of surgery (no operation or less extensive procedures) correlates with advancing age. There is a trend for less breast conserving surgery and fewer reconstruction procedures, perhaps based on the questionable belief that older women do not have the same concerns about body image.[2] Encouragingly, there seems to be a trend for increased surgical treatment and survival of elderly patients in recent years.[15]

Radiotherapy

Radiotherapy is used less often in elderly patients, although its safe use, without increased toxicity, has been described in this population. This includes radical radiotherapy in pelvic malignancies and radiotherapy of curative intent in thoracic cancers.[16 17] Transport for elderly patients can be a problem,[3] and protocols to reduce hospital visits can be designed.[18] Elderly patients receive more palliative than curative radiotherapy, but decisions on treatment protocols are not influenced by chronological age once the patient has been referred to a radiotherapist.[19]

Hormonal therapy

Tamoxifen may offer great benefit in elderly patients with breast cancer. It has been used as sole therapy after reports that this produced survival equivalent to surgery and tamoxifen combined. Further follow up showed a high local recurrence rate in the tamoxifen group, with many women requiring salvage surgery or radiotherapy. Tamoxifen alone therefore can no longer be recommended as optimum treatment for older women.[20] Newer hormonal treatments for breast cancer, such as anastrozole, can also be used in elderly women. Carcinoma of the prostate is responsive to hormonal treatments such as goserelin, which are useful in elderly patients.

Adjuvant therapy

Adjuvant treatments have proved benefit in breast and colorectal cancer, which are common in elderly patients. There are no data on their use in the elderly population, but where normal life expectancy exceeds the survival benefit of treatment, there is no reason why such treatments could not be employed.[21]

Palliative care

Increasing age is an independent predictor of inadequate pain management. Fear of addiction to

opioids, the belief that "good" patients do not complain of pain, and concern that treatment of pain will distract effort from treating the cancer are examples of patient related barriers to the management of cancer pain: older patients are more likely to have these concerns. Family caregivers may have similar concerns, and their views can influence successful pain control. Cognitively impaired elderly patients may underreport pain, but their complaints of pain are no less valid than those of cognitively intact individuals. Pain, as well as other symptoms such as fatigue and dyspnoea, may be caused by comorbid conditions and not the cancer or its treatment. A search for other treatable conditions is especially important in elderly patients.[22]

Screening

Some cancers can be diagnosed at an early stage by screening. There are different screening policies in different countries, particularly for prostate and colorectal cancers. Screening for these cancers is available in the United States but not in the United Kingdom, although screening for colorectal cancer is now being considered.

Established screening programmes for breast and cervical cancers have upper age limits. For cervical carcinoma, if a woman over 65 has an adequate screening history with at least three consecutive negative smears, further screening is inefficient and can stop. However, many older women have never had a smear and may still benefit from screening.[23] The breast screening programme in the United Kingdom invites women for mammography up to the age of 65 and allows women older than this to be screened on request. However, many older women are not aware of this, and many do not realise that they are at risk.[24] Routine screening with no upper age limit may save lives.[25] Breast examination is often not performed in elderly women, although most would be willing to undergo this.[26]

Patient issues

Some elderly patients may decide not to accept recommended investigations or interventions. Others are as likely to agree to chemotherapy as their younger counterparts, though there are differences in their assessment of risk-benefit ratios for more toxic regimens.[27] A survey of elderly people's attitudes to invasive procedures showed that most would want investigations and treatments for life threatening illnesses.[28] Psychologically, elderly people fare no worse than the young; indeed they may cope better with a diagnosis of cancer.[29] There are many myths about cancer—for example, that surgery spreads cancer or that cancer treatments are worse than the disease—though belief in these myths and level of knowledge about cancer seem to be related more to previous educational level and social class than to age.[30]

Issues for healthcare staff

Ageist attitudes persist among healthcare staff.[31] There is reduced referral to specialists with increasing age, though the rationale behind this is not clear.[32] Doctors are poor at judging the health related quality of life of their elderly patients, and they frequently grade this lower than patients do themselves.[33] Older people may be more likely to follow their doctor's recommendations without question, but the way in which treatment options are presented can influence their choice. Lack of knowledge about the ageing process among doctors may also be a problem. Some may be unaware that a 75 year old woman has a life expectancy of 11.1 years and that of a 75 year old man 8.5 years. To help overcome this, there has been a move in the United States to integrate geriatric medicine into the subspecialties of medicine, particularly oncology.[34]

Cancer services

There is wide variation in practice for most cancers between different specialists, hospitals, and regions.[35] The Calman/Hine report on the organisation of cancer services in the United Kingdom[36] recommends that cancer care should be delivered by specialists working in designated cancer units and centres. With increased specialisation, there is a need for interdisciplinary teams. Evidence is increasing that care organised in this way improves outcomes, and it seems reasonable to expect that this should apply equally to elderly patients.[37]

Conclusions

The problems of cancer in old age have been the topic of several editorials and feature articles.[38–40] Cancer in old age is not managed the same way as in younger people, and the differences are not wholly explained by appropriate adjustment for the condition of the individual patients. We do not know which variables predominantly influence decision making[38]—is it the patient's or family's acceptance of therapy or the physician's opinions (including possible bias based on chronological rather than biological age alone)? Adjustments are made for comorbidity and functional status, but it is not clear how these are measured in practice. Understanding which criteria are used in making treatment decisions is necessary. It is possible that healthcare professionals are delivering a poor standard of care to some elderly cancer patients.

Where do we go from here? Firstly, we should identify what patients and doctors know about the investigations and cancer treatments that are effective in and acceptable to older people. Secondly, we need answers on how best to manage common cancers in old age, especially breast, colorectal, lung, and prostate cancers. This must include data on disability, handicap, health related quality of life, and psychological well-being as well as physical outcome measures.

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1 Trimble EL, Carter CL, Cain D, Freidlin B, Ungerleider RS, Friedman MA. Representation of older patients in cancer treatment trials. *Cancer* 1994;74:2208-14.
2 Busch E, Kemeny M, Fremgen A, Osteen RT, Winchester DP, Clive RE. Patterns of breast cancer care in the elderly. *Cancer* 1996;78:101-11.
3 Goodwin JS, Hunt WC, Samet JM. Determinants of cancer therapy in elderly patients. *Cancer* 1993;72:594-601.
4 Guadagnoli E, Weitberg A, Mor V, Silliman RA, Glicksman AS, Cummings FJ. The influence of patient age on the diagnosis and treatment of lung and colorectal cancer. *Arch Intern Med* 1990;150: 1485-90.
5 Ries LA. Ovarian cancer. Survival and treatment differences by age. *Cancer 1993;71:524-9.*
6 Samet J, Hunt WC, Key C, Humble CG, Goodwin JS. Choice of cancer therapy varies with age of patient. *JAMA* 1986;255:3385-90.

7 Forman D, Rider L, eds. *Yorkshire Cancer Registry report 1996*. Leeds: Yorkshire Cancer Organisation, 1996.
8 Campbell AJ, Buchner DM. Unstable disability and the fluctuations of frailty. *Age Ageing* 1997;26:315-8.
9 Balducci L, Mowrey K, Parker M. Pharmacology of antineoplastic agents in older patients. In: Balducci L, Lyman GH, Ershler WB, eds. *Geriatric oncology*. Philadelphia: JB Lippincott Co, 1992:169-80.
10 Shank WA, Jr., Balducci L. Recombinant hemopoietic growth factors: comparative hemopoietic response in younger and older subjects. *J Am Geriatr Soc* 1992;40:151-4.
11 Begg CB, Carbone PP. Clinical trials and drug toxicity in the elderly. The experience of the Eastern Cooperative Oncology Group. *Cancer* 1983;52:1986-92.
12 Evans WK, Radwi A, Tomiak E, Logan DM, Martins H, Stewart DJ, et al. Oral etoposide and carboplatin. Effective therapy for elderly patients with small cell lung cancer. *Am J Clin Oncol* 1995;18:149-55.
13 Morandi U, Stefani A, Golinelli M, Ruggiero C, Brandi L, Chiapponi A, et al. Results of surgical resection in patients over the age of 70 years with non small-cell lung cancer. *Eur J Cardiothorac Surg* 1997;11:432-9.
14 Bufalari A, Ferri M, Cao P, Cirocchi R, Bisacci R, Moggi L. Surgical care in octogenarians. *Br J Surg* 1996;83:1783-7.
15 Farrow DC, Hunt WC, Samet JM. Temporal and regional variability in the surgical treatment of cancer among older people. *J Am Geriatr Soc* 1996;44:559-64.
16 Pignon T, Gregor A, Schaake KC, Roussel A, Van Glabbeke M, Scalliet P. Age has no impact on acute and late toxicity of curative thoracic radiotherapy. *Radiother Oncol* 1998;46:239-48.
17 Pignon T, Horiot JC, Bolla M, van Poppel H, Bartelink H, Roelofsen F, et al. Age is not a limiting factor for radical radiotherapy in pelvic malignancies. *Radiother Oncol* 1997;42:107-20.
18 Rostom AY, Pradhan DG, White WF. Once weekly irradiation in breast cancer. *Int J Radiat Oncol Biol Phys* 1987;13:551-5.
19 Olmi P, Ausili-Cefaro G. Radiotherapy in the elderly: a multicentric prospective study on 2060 patients referred to 37 Italian radiation therapy centers. *Rays* 1997;22:53-6.
20 Robertson JF, Todd JH, Ellis IO, Elston CW, Blamey RW. Comparison of mastectomy with tamoxifen for treating elderly patients with operable breast cancer. *BMJ* 1988;297:511-4.
21 Balducci L, Extermann M, Fentiman I, Monfardini S, Perrone F. Should adjuvant chemotherapy be used to treat breast cancer in elderly patients (≥70 years of age)? *Eur J Cancer* 1997;33:1720-4.
22 Cleary JF, Carbone PP. Palliative medicine in the elderly. *Cancer* 1997;80:1335-47.
23 Fletcher A. Screening for cancer of the cervix in elderly women. *Lancet* 1990;335:97-9.
24 Age Concern. *Not at my age: why the present breast screening system is failing women aged 65 or over*. London: Age Concern England, 1996.
25 Van Dijck JA, Verbeek AL, Beex LV, Hendriks JH, Holland R, Mravunac M, et al. Mammographic screening after the age of 65 years: evidence for a reduction in breast cancer mortality. *Int J Cancer* 1996;66:727-31.
26 Haigney E, Morgan R, King D, Spencer B. Breast examinations in older women: questionnaire survey of attitudes of patients and doctors. *BMJ* 1997;315:1058-9.
27 Yellen SB, Cella DF, Leslie WT. Age and clinical decision making in oncology patients. *J Natl Cancer Inst* 1994;86:1766-70.
28 Mead GE, Pendleton N, Pendleton DE, Horan MA, Bent N, Rabbit P. High technology medical interventions: what do older people want? *J Am Geriatr Soc* 1997;45:1409-11.
29 Given CW, Given BA, Stommel M. The impact of age, treatment, and symptoms on the physical and mental health of cancer patients. A longitudinal perspective. *Cancer* 1994;74:2128-38.
30 Weinrich SP, Weinrich MC. Cancer knowledge among elderly individuals. *Cancer Nurs* 1986;9:301-7.
31 Wetle T. Age as a risk factor for inadequate treatment. *JAMA* 1987;258:516.
32 Newcomb PA, Carbone PP. Cancer treatment and age: patient perspectives. *J Natl Cancer Inst* 1993;85:1580-4.
33 Pearlman RA, Uhlmann RF. Quality of life in chronic diseases: perceptions of elderly patients. *J Gerontol* 1988;43:M25-30.
34 Hazzard WR, Woolard N, Regenstreif DI. Integrating geriatrics into the subspecialties of internal medicine: the Hartford Foundation/American Geriatrics Society/Wake Forest University Bowman Gray School of Medicine initiative. *J Am Geriatr Soc* 1997;45:638-40.
35 Sainsbury R, Rider L, Smith A, MacAdam A. Does it matter where you live? Treatment variation for breast cancer in Yorkshire. The Yorkshire Breast Cancer Group. *Br J Cancer* 1995;71:1275-8.
36 Calman K, Hine D. *A policy framework for commissioning cancer services. A report by the Expert Advisory Group on Cancer to the Chief Medical Officers of England and Wales. 1995*. London: Department of Health, 1995.
37 Selby P, Gillis C, Haward R. Benefits from specialised cancer care. *Lancet* 1996;348:313-8.
38 Monfardini S. What do we know on variables influencing clinical decision-making in elderly cancer patients? *Eur J Cancer* 1996;32A:12-4.
39 Fentiman IS. Are the elderly receiving appropriate treatment for cancer? *Ann Oncol* 1996;7:657-8.
40 Coebergh JW. Significant trends in cancer in the elderly. *Eur J Cancer* 1996;32A:569-71.

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Methods in health services research

Interpreting the evidence: choosing between randomised and non-randomised studies

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Evaluations of healthcare interventions can either randomise subjects to comparison groups, or not. In both designs there are potential threats to validity, which can be external (the extent to which they are generalisable to all potential recipients) or internal (whether differences in observed effects can be attributed to differences in the intervention). Randomisation should ensure that comparison groups of sufficient size differ only in their exposure to the intervention concerned. However, some investigators have argued that randomised controlled trials (RCTs) tend to exclude, consciously or otherwise, some types of patient to whom results will subsequently be applied. Furthermore, in unblinded trials the outcome of treatment may be influenced by practitioners' and patients' preferences for one or other intervention. Though non-randomised studies are less selective in terms of recruitment, they are subject to selection bias in allocation if treatment is related to initial prognosis.

These issues have led to extensive debate, although empirical evidence is limited. This paper is a brief summary of a more detailed review[1] of the impact of these potential threats.

Summary points

Treatment effects obtained from randomised and non-randomised studies may differ, but one method does not give a consistently greater effect than the other

Treatment effects measured in each type of study best approximate when the exclusion criteria are the same and where potential prognostic factors are well understood and controlled for in the non-randomised studies

Subjects excluded from randomised controlled trials tend to have a worse prognosis than those included, and this limits generalisability

Subjects participating in randomised controlled trials evaluating treatment of existing conditions tend to be less affluent, educated, and healthy than those who do not; the opposite is true for trials of preventive interventions