

Problem Solving in Older Cancer Patients

ALISTAIR RING, DANIELLE HARARI
 TANIA KALSI, JANINE MANSI
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Problem Solving in Older Cancer Patients

If to be human is to be limited, then the role of caring professions and institutions – from surgeons to nursing homes – ought to be aiding people in their struggle with those limits. Sometimes we can offer a cure, sometimes only a salve, sometimes not even that. But whatever we can offer, our interventions, and the risks and sacrifices they entail, are justified only if they serve the larger aims of a person's life. When we forget that, the suffering we inflict can be barbaric. When we remember it the good we do can be breathtaking.

Atul Gawande

Being Mortal: Medicine and What Matters in the End, 2014

Problem Solving in Older Cancer Patients

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Preface

The cancer care community of patients, healthcare professionals, scientists, managers and charity workers, as well as the general public, are becoming increasingly aware of how vital it will be to plan thoroughly to meet the needs of the growing number of older people who will be living with cancer now and in the future. Not only will the number of cases increase but it will be essential for healthcare services to ensure that diagnostic approaches, treatments and care are satisfactorily tailored to meet the needs and choices of individuals who are at higher risk of comorbidities and frailty. We must avoid the pitfall of tailoring our approaches to individuals based on their chronological age: our approaches must fit with all the needs of older patients, from their financial outlook through to the support they can or cannot access, as well as their medical fitness.

Macmillan Cancer Support and Cancer Research UK were pleased to support the Association of Cancer Physicians and the British Geriatrics Society in their 2014 workshop held in Manchester and in this publication, *Problem Solving in Older Cancer Patients*. Experts from the UK and abroad have provided perspectives on the important issues and challenges that we face in providing the right approaches to the diagnosis and care of older cancer patients. Importantly, the workshop and book are very patient-centred and focus on over 30 individual cases. The knowledge and skills of oncologists and geriatricians of all professions – established professionals as well as those in training – are brought to bear on individual cases. This integrated approach to the preparation of the book should help to ensure future integrated approaches in clinical care across the UK.

Experts have identified areas where we can learn from other countries, especially those in mainland Europe that have specific initiatives for the care of older cancer patients. The importance of innovation and research to allow us to find better ways of diagnosing and managing cancer in older people has been emphasized and is welcomed. The workshop and the book have highlighted the importance of the many different groups of healthcare professionals who together are responsible for caring for cancer patients and older people. Different professional groups often have different styles and different cultures but they all share the aim of bringing about the best outcomes, the best quality of life and the best experience for their patients. We anticipate that this new text will be a useful contribution to improving planning for the care of cancer patients and the development of clinical care teams from oncology, geriatrics, primary care and many others to deploy their skills for the maximum benefit of this important group of patients.

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Abbreviations

AAA	Abdominal aortic aneurysm	ER	Oestrogen receptor
ACP	Association of Cancer Physicians	ESMO	European Society for Medical Oncology
ADL	Activities of daily living	ETF	Elderly Task Force
ADT	Androgen deprivation therapy	EVAR	Endoscopic repair of abdominal aortic aneurysm
AF	Atrial fibrillation	FIGO	International Federation of Gynecology and Obstetrics
AHP	Allied health professional	FOLFIRI	Folinic acid, fluorouracil, irinotecan
AML	Acute myeloid leukaemia	FOLFIRINOX	Folinic acid, fluorouracil, irinotecan, oxaliplatin
ASA	American Society of Anesthesiologists	FOLFOX	Folinic acid, fluorouracil, oxaliplatin
BNP	B-type natriuretic peptide	5-FU	Fluorouracil
BPH	Benign prostatic hypertrophy	GCSF	Granulocyte colony-stimulating factor
BSC	Best supportive care	GFR	Glomerular filtration rate
CAPOX	Capecitabine, oxaliplatin	GIST	Gastrointestinal stromal tumour
CCG	Clinical commissioning group	GOJ	Gastro-oesophageal junction
CDI	<i>Clostridium difficile</i> infection	GTN	Glyceryl trinitrate
CGA	Comprehensive Geriatric Assessment	HER2	Human epidermal growth factor receptor 2
CHOP	Cyclophosphamide, doxorubicin, vincristine, prednisolone	HNA	Holistic Needs Assessment
CK	Cytokeratin	IADL	Instrumental activities of daily living
CMF	Cyclophosphamide, methotrexate and fluorouracil	IMCA	Independent mental capacity advocate
COPD	Chronic obstructive pulmonary disease	LDH	Lactate dehydrogenase
CUP	Cancer of unknown primary	LMWH	Low-molecular-weight heparin
DCIS	Ductal carcinoma <i>in situ</i>	LPA	Lasting Power of Attorney
DLBCL	Diffuse large B cell lymphoma	LVEF	Left ventricular ejection fraction
DRE	Digital rectal examination	MCA	Mental Capacity Act 2005
EBRT	External beam radiation therapy	MDT	Multidisciplinary team
ECOG	Eastern Cooperative Oncology Group	MET	Metabolic equivalent of task
ECX	Epirubicin, cisplatin, capecitabine	MIBC	Muscle-invasive bladder cancer
eGFR	Estimated glomerular filtration rate	mpMRI	Multiparametric magnetic resonance imaging
EGFR	Epidermal growth factor receptor		
EORTC	European Organisation for Research and Treatment of Cancer		

mRCC	Metastatic renal cell carcinoma	TTF	Thyroid transcription factor
MUO	Malignancy of unidentified primary origin	UTI	Urinary tract infection
NCEI	National Cancer Equality Initiative	VEGF	Vascular endothelial growth factor
NHSCB	NHS Commissioning Board	VTE	Venous thromboembolism
NSAIDs	Non-steroidal anti-inflammatory drugs	XELIRI	Capecitabine, irinotecan
NSCLC	Non-small-cell lung carcinoma		
NTproBNP	N-terminal pro-B-type natriuretic peptide		
NYHA	New York Heart Association		
OAB	Overactive bladder		
OH	Orthostatic hypotension		
OS	Overall survival		
OSA	Obstructive sleep apnoea		
PD-1	Programmed cell death protein 1		
PFS	Progression-free survival		
POI	Pharmaceutical Oncology Initiative		
PS	Performance status		
PSA	Prostate-specific antigen		
PVD	Peripheral vascular disease		
R-CHOP	Rituximab, cyclophosphamide, doxorubicin, vincristine, prednisolone		
RCT	Randomized controlled trial		
RFA	Radiofrequency ablation		
R-mini-CHOP	Full-dose rituximab, low-dose cyclophosphamide, doxorubicin, vincristine, prednisolone		
ROC	Receiver operating characteristic		
SACT	Systemic anticancer therapy		
SIOG	International Society of Geriatric Oncology		
SNP	Single nucleotide polymorphism		
SSRI	Selective serotonin reuptake inhibitor		
TIA	Transient ischaemic attack		
TKI	Tyrosine kinase inhibitor		
TSH	Thyroid-stimulating hormone		

01 Cancer in Older People: an Overview

Catherine Handforth, Nicola Turner, David Jackson, Andrew Clegg, Peter Hall, Katie Spencer, Geoff Hall, Mark Lawler, Peter Selby

There is increasing discussion about service needs and developments for cancer care for older people. The topic is not new.¹⁻⁴ In the USA, the population aged 65 or over will double by 2050, and, in the EU, people over 65 years will outnumber children by 2060.^{5,6} In the UK, by 2030, about 70% of cancers will occur in people aged over 65 years.⁷ Studies by the International Cancer Benchmarking Partnership and EUROCARE, the European Cancer Registry, suggest that the survival gap is widening between older and younger patients diagnosed with cancer in Europe.⁸⁻¹⁰ There are also worrying indications from within these studies that older patients in the UK may be relatively disadvantaged.⁸⁻¹¹

Improvements in the care of older patients with cancer will ultimately depend on revisiting the biology underlying cancer in older patients. This is because fundamental biological questions about the relationship between ageing and cancer remain poorly understood, requiring a deeper understanding of processes such as cellular senescence, DNA damage and genomic instability, telomere biology, autophagy, and cellular responses to metabolic and oxidative stress.¹²⁻¹⁴ Currently at a clinical practice level, however, it is very clear that older patients are disadvantaged in their access to systemic therapy, radiotherapy and surgery: the main modalities of anticancer therapy.

Systemic therapy in the forms of cytotoxic chemotherapy and biological agents has a role to play in most tumour types. Current evidence, however, suggests that older patients are undertreated, as chronological age remains an independent factor for the use of chemotherapy, even when adjustments are made for comorbidity and frailty. This lack of equity in access and uptake of cancer care may lead to worse outcomes in older cancer patients. For example, more than 70% of cancer deaths occur in men aged over 75 with prostate cancer, yet few older patients receive treatment for localized prostate cancer. In the majority of cases, older patients are denied access to chemotherapy for advanced disease, which if carefully selected can confer benefits with avoidable toxicity.¹⁵ Colorectal cancer is another disease of the older adult, yet again the evidence suggests that optimal therapy is not always being provided to these patients.¹⁶ A significant proportion of older women with triple-negative breast cancer receive less chemotherapy than their younger counterparts, despite the available evidence demonstrating its increased efficacy. Older women may also receive less endocrine therapy than their younger counterparts with breast cancer.¹⁷⁻¹⁹ Specifically in the UK, a National Cancer Equality Initiative (NCEI)/Pharmaceutical Oncology Initiative (POI) joint report concluded that ‘clinicians may over rely on chronological age as a proxy for other factors, which are often but not necessarily associated with age, e.g. comorbidities, frailty’.²⁰ An NHS England publication²¹ entitled *Are older people receiving cancer drugs?* (published in 2013) demonstrated considerable variation in the use of systemic anticancer therapy in older people and concluded: ‘It does not seem plausible that differences in referral patterns or the age profile of populations served by hospitals could alone explain the variation. The reason for this variation requires further exploration. It seems likely that some variation at least will be caused by the use of age as a proxy for clinical factors, rather than differences in patient health status or preference.’

Despite the importance of appropriate radiation treatment in all cancer patients, including older patients, the uptake of this treatment is relatively low.²² There are relatively few trials specifically conducted in this population; nonetheless, it is clear that any consideration of radiotherapy in older patients must take into account the altered loco-regional tumour behaviour in older patients with several tumour types, the impact of comorbidities and the impact of diminished functional reserve.²²

Surgery remains the most important curative modality for cancer patients and is appropriate for many older patients. The evidence to support decision making in this age group remains limited, but Korc-Grodzicki and colleagues²³ have emphasized that ‘chronological age alone should not be a determinant for treatment decisions’. Older patients benefit from careful preoperative assessment, which should evaluate functional ability, comorbid conditions, polypharmacy, cognition, nutritional status and frailty in order to determine the risk of adverse events. In some situations, a period of multidisciplinary intervention prior to surgery may improve outcomes. This could include medication review, a cardiopulmonary exercise programme, nutritional supplements or physiotherapy assessment.

Recognizing the disparities that exist for cancer care in older people, the European Organisation for Research and Treatment of Cancer (EORTC) established an EORTC Cancer in the Elderly Task Force, with the stated aim of improving access to clinical trials and research in order to deliver optimum standards of care for the geriatric population. A joint position paper between the EORTC, the Alliance for Clinical Trials in Oncology and the International Society of Geriatric Oncology has recently been published, specifying a roadmap for research and clinical trials in older people and emphasizing the absolute requirement for clinical trials to be without an upper age limit, thus removing a critical barrier for the eligible older patient.^{24,25} They also recommend the need for standardized approaches to the measurement of frailty and comorbidity in trials and practice.²⁴ In the UK, the publication of the NCEI/POI joint report highlighted above²⁰ has been part of a concerted recent effort to redress the balance in favour of the older cancer patient, culminating in the launch of an ‘Action for the Elderly in Cancer’ initiative as the main priority of the NCEI at the Britain Against Cancer Conference in London (2014). Although geriatric oncology is beginning to become established as a specialty in North America and Europe, this specialist approach is not yet widely available in the UK.

In older cancer patients, the identification of frailty may be especially important to help guide appropriate, shared decision making, irrespective of what treatment is being considered. Frailty is common in older cancer patients and is independently associated with an increased risk of adverse outcomes, including cancer-related mortality, postoperative complications and poor tolerance of chemotherapy. It has also been identified as a better discriminator of those at risk of adverse outcomes in the surgical and community settings. There are available tools to assess frailty in older patients and inform decisions on therapy, but they are not routinely used in oncology. There is no consensus as to which assessment method should be used to identify frailty in older cancer patients, and a variety of methods have been used in the small number of published trials to date.²⁶

In order to make progress, we need a patient-centred, multidisciplinary approach to the care of every older cancer patient. This should not be based solely on chronological age but should also include assessment of frailty, comorbidity and patient choice. Where appropriate, we should develop new treatment approaches that are well tolerated in older people and maximize clinical research activity in older cancer patients. These may include methods to stratify trial participants on the basis of frailty and to maximize the transferability of evidence from trials in younger patients to older populations, for example by appropriate baseline assessment to allow regression-based

adjustment; and running parallel observational ‘current practice’ studies alongside trials. In the absence of evidence from randomized controlled trials, evidence-based medicine has not become routine or possible for many older cancer patients. In some settings, alternatives to randomized trials may become essential. There is a need for the development and application of geriatric decision-making tools and their recognition and routine use in oncology, and to ensure that the principle of early diagnosis (underpinning more effective and less aggressive therapy) is applied in older patients as well as in their younger counterparts.

The provision of individualized treatment to older cancer patients may require upfront expenditure but is likely to provide benefits in terms of improved quality of life and survival, fewer treatment complications and use of resources, and could also help to maintain independence. In order to achieve this, the integration of health and social care services for older cancer patients will be vital. In addition to tailored treatment programmes, we must also consider individual patient preferences and priorities regarding treatment acceptability and tolerability. These are often different in older cancer patients compared with their younger counterparts.

The approaches that are developed towards managing cancer in older people will have a profound impact on future cancer policy and outcomes. While cancer survivorship is increasing overall, with the most recent figures indicating 11.7 million cancer survivors in the USA and nearly 14 million in Europe, the percentage is lower in older people compared with the overall population. Thus, cancer survivorship may plateau, or even decline, unless we develop better approaches for the management of older cancer patients.

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PERSPECTIVE

02 Clinical Epidemiology and Patterns of Care for Cancer in Older Patients

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Background

Cancer is predominantly a disease of older people. With an ageing population, this poses a major challenge to healthcare systems. In 1985, around 15% of the UK population was over the age of 65, but by 2010 this proportion had increased, by an additional 1.7 million people, to 17% of the population.¹ This trend is set to continue, and it is projected that by 2035 more than 23% of the population will be over 65.¹

Cancer incidence is highest in older people, with 63% of all cancers diagnosed in those aged 65 or over.² Figure 2.1 shows the increasing incidence of cancer in individuals aged 65 and over between 1971 and 2009. It is anticipated that there will continue to be large increases in the number of older people diagnosed with cancer over the forthcoming decades.² By 2040, it is estimated that almost a quarter of people over the age of 65 will have experienced the disease (amounting to 4.1 million people).³ As such, ensuring that high-quality services are available to care for this rapidly growing population is a major challenge for healthcare providers.

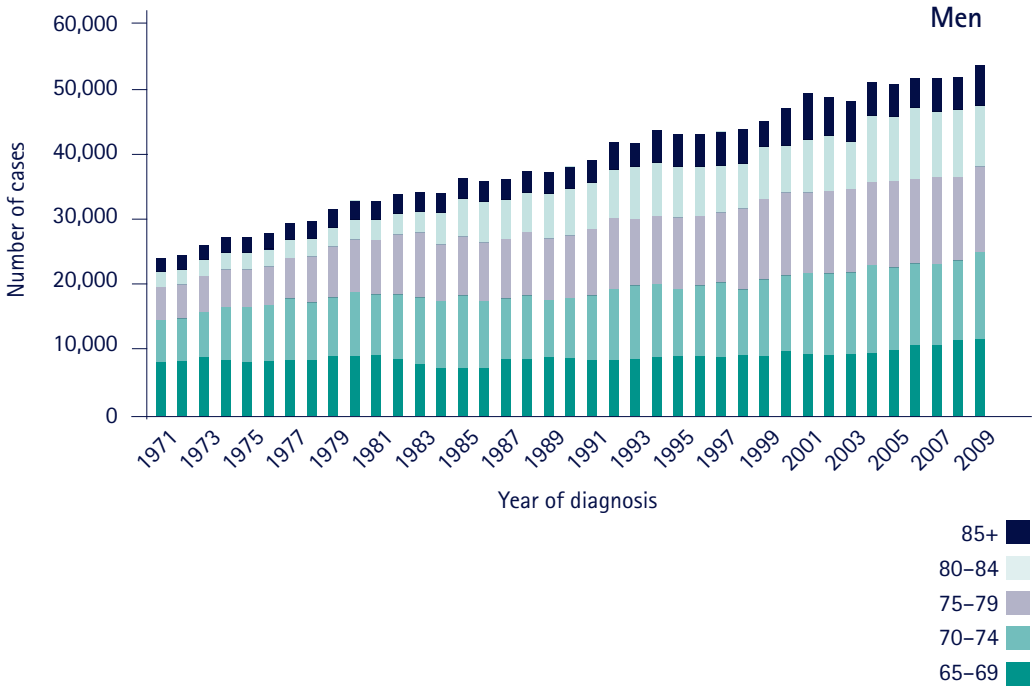
The scale of the challenge is compounded when it is considered alongside current concerns that those diagnosed in older age groups are experiencing inequalities and inequities in both their care and prognosis.⁴⁻⁶ These anxieties have been heightened by international comparisons repeatedly showing that the 5 year cancer survival rates attained in the UK lag behind those of many economically comparable countries, due to poorer outcomes for older patients.⁷⁻¹¹ There is also a growing body of evidence suggesting that older patients are undertreated and do not have access to the best care.⁷ Improving outcomes for older patients has, therefore, become a priority; but, before steps can be taken to reduce the deficits, it is important to understand how they have arisen. The available evidence suggests that a number of factors, across the entire care pathway, may be responsible.

Diagnosis and presentation

First, there appear to be differences in relation to diagnosis and presentation.^{6,12} The best outcomes for solid tumours are achieved when individuals are diagnosed with early-stage disease.¹³ It is unfortunate, therefore, that it appears that a greater proportion of older patients present with advanced disease compared with younger patients.^{14,15}

A greater proportion of older patients also present as emergencies.¹⁶ A national population-based study of all cancer patients over a 5 year period in England identified that 15% of those under the age of 50 had presented as an emergency, which rose to 43% in those over 85.¹⁶ A recent systematic review confirmed this effect for lung and colorectal cancer.¹² Emergency presentation is known to be associated with a more advanced stage of cancer;¹⁶ however, even after adjustment for this, there remain poorer outcomes¹⁷ and lower rates of treatment with curative intent.¹⁸

Colorectal, lung and prostate cancer



Colorectal, lung and breast cancer

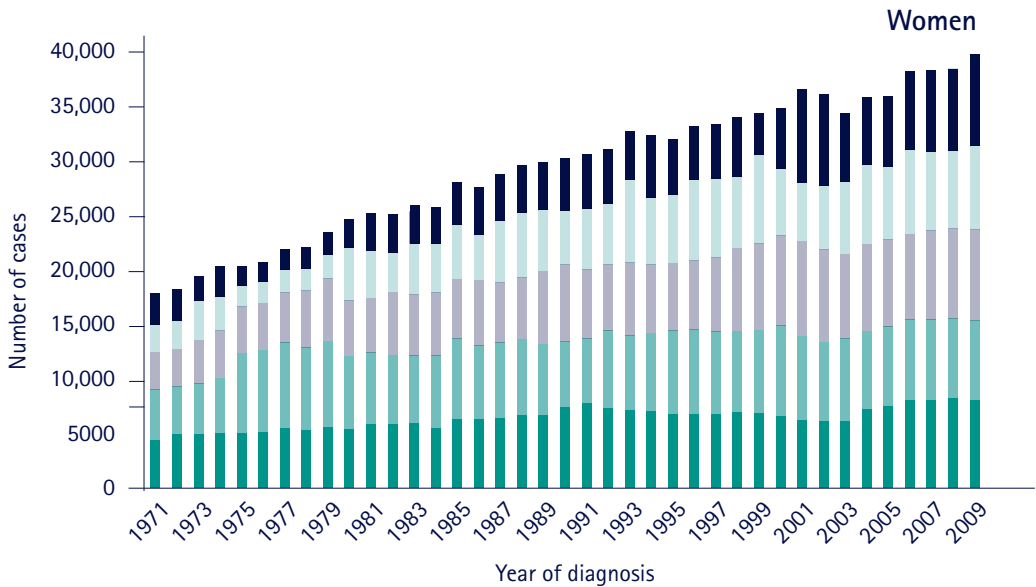


Figure 2.1 Registrations in England, between 1971 and 2009, of newly diagnosed colorectal, lung and prostate cancers in men, and of newly diagnosed colorectal, lung and breast cancers in women (adapted from Sinha *et al.*⁵⁶).

Reasons behind these differing diagnostic pathways in older people are not fully understood but may include lack of awareness of cancer symptoms, differing symptomatology, lack of social support and variation in help-seeking behaviour.

Management

After diagnosis, age-related differences persist in the management of cancer. Surgery is the main curative treatment option for the majority of individuals with solid tumours, but it appears that surgical intervention rates are significantly reduced in older people.^{6,19–21} Similarly, age-related inequalities are apparent in the use of both chemotherapy^{5,6,22} and radiotherapy.⁶ This variation in practice has caused significant concern and led some to argue that older people are facing discrimination and being denied access to potentially curative treatment.⁴ However, this variation in treatment may be clinically appropriate.^{23–26} Two of the most important confounding factors may be the presence of comorbid disease and frailty, both of which are known to increase with age (Figure 2.2).^{27–32} Both can reduce physiological reserve, increasing the complexity of cancer management and potentially making individuals unsuitable for treatment. Studies have suggested that, whilst some older patients may not be fit enough for standard treatment, they may benefit from adapted treatment regimens.^{33–36} Quantifying the impact of these factors is vitally important to assess whether true inequities exist, but it is also extremely difficult with the population-based data currently available.

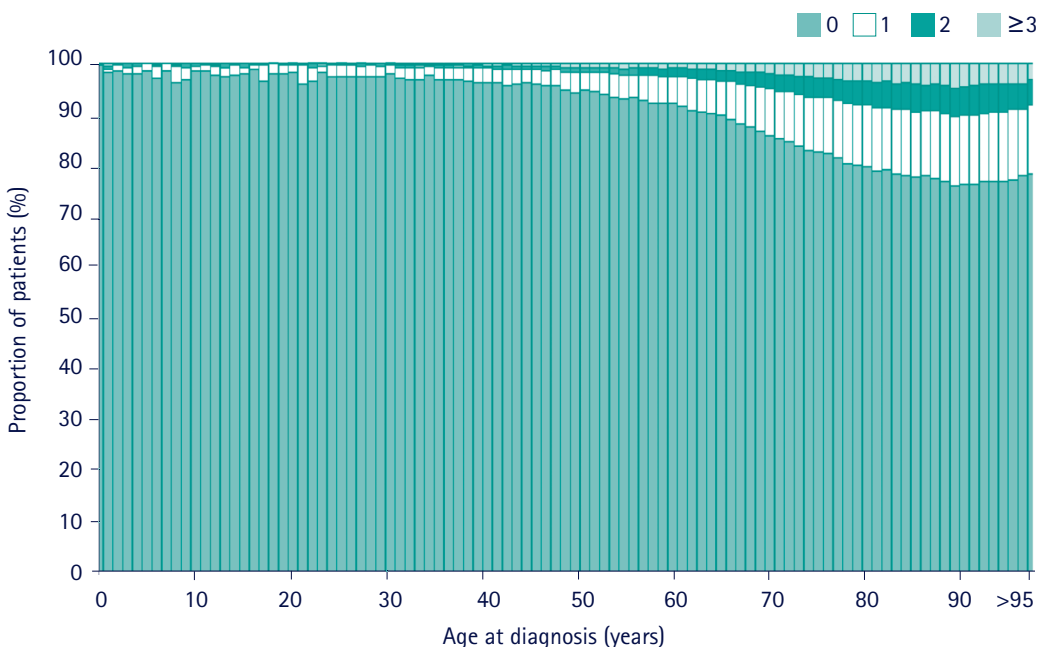


Figure 2.2 Charlson Comorbidity Index scores of patients diagnosed with cancer in England between 2006 and 2010 (all cancers excluding non-melanoma skin cancer). Diagnostic data for comorbidities provided by inpatient Hospital Episode Statistics records, matched at a patient level to cancer registration records and supplied by the National Cancer Registration Service (www.ncr.nhs.uk).

Comorbidity and frailty

Objective tools to measure burden of comorbidity are available. The Charlson Comorbidity Index³⁷ and Elixhauser Comorbidity Measure³⁸ have been used to quantify levels of comorbidity using routinely available data. They tend, however, to capture only the more severe illnesses and, consequently, only provide a relatively crude indicator of the extent of any concomitant illness.^{39,40} Epidemiological studies using these indices tend to suggest, therefore, that comorbidity does not explain all the age-related variation in care observed.⁴¹ More rigorous population-based comorbidity data are required to determine whether this variation is inequitable.

The situation is similar with respect to frailty. To date, no national epidemiological analyses have been able to assess the contribution of frailty to age-related variation in care and outcome. A number of frailty indices exist,⁴² but none are available that enable the extent of the condition to be quantified via routine data at a population level. Higher resolution prospective studies have assessed comorbidity and functional status in greater depth; however, despite this, variation in treatment with chronological age persists.⁴³ Frailty is such an important factor to consider in analyses that further evidence quantifying its presence across the population is urgently needed.

Outcomes

Survival

Age-related differences in management pathways exist in parallel with significant age-related differences in outcome. The best indicator of the effectiveness of a cancer care system is the survival of the individuals it treats. Unfortunately, when comparing survival rates across age groups, both within the UK⁴⁴ and internationally,^{8,11,45–47} significant differences are observed. In England, after adjusting for deaths due to other causes, the lowest overall 5 year cancer survival rate is observed in those over the age of 80.⁴⁸ Again, many factors may contribute to these outcome differences, including underlying differences in tumour biology and patient behaviour, lower active treatment rates and differing levels of comorbidity and frailty. To determine the true extent of any age-related inequalities or inequities it is important to gain a better understanding of how these factors interact with age.

Patient experience and quality of life

Whilst there are undoubtedly lower treatment rates in older people, NHS England's National Cancer Patient Experience Survey suggests that older patients actually report, overall, a more positive experience of their care compared with younger patients.⁴⁹ These annual patient experience surveys have indicated that older age groups were more likely to feel they had been treated with dignity and respect and felt their views were taken into consideration when making treatment decisions.⁴⁹ By no means were all the aspects of care included in the survey found to be better in the older age groups: for example, the proportion of older people who felt they had adequate information about side effects was lower than for younger ages, but generally the older English cancer population report a good patient experience.

Another area of cancer care where there are fewer obvious inequalities with respect to older people is around the health-related quality of life of survivors. Large surveys using population-based sampling approaches suggest that older people actually report better health-related quality of life than those in the youngest age groups.^{50,51} Again, understanding exactly what is driving these differences is complex, as many of the factors strongly predictive of a worse health-related

quality of life are correlated with increasing age. Further evidence is again, therefore, required to fully understand the relationship and ensure that the needs of the growing population of older cancer survivors are met.

Clinical trials

The best medical evidence via which to determine this, and, hence, generate the gold standard treatment pathways for older patients, would be derived from randomized controlled trials. Unfortunately, however, older people are often underrepresented in such studies and, as a result, the current evidence base to inform optimal cancer management in older people is somewhat limited.^{27,52,53} Furthermore, the individuals entered into such studies, particularly those who are older, may not be entirely representative of the population at large, as trials tend to recruit younger, more affluent people with better prognosis disease and low levels of comorbidity and frailty.⁵⁴ So, again, extrapolating the findings of these studies to inform the optimal management of the older population may be misleading. Assessment of treatment benefit in older people tends, therefore, to rely on data gathered from observational studies. However, the analysis of such observational data to generate robust conclusions is methodologically difficult. Failure to consider or make adjustment for confounding variables can lead to biased results. A recent systematic review determined that such methodological mistakes were common.⁵⁵

Conclusion



It is clear that major differences exist, at a population level, in both cancer management and outcomes in older people. The currently available epidemiological evidence would strongly suggest that care is inequitable, but, in the absence of stronger data on many of the poor prognostic factors (such as stage, emergency presentation, comorbidity and frailty) correlated with age, it is difficult to draw firm conclusions. Further evidence is, therefore, urgently needed. It must be borne in mind, however, that epidemiology is the study of disease in a population and not individuals. Every person is different and healthcare providers must seek to ensure that they do not make assumptions about any individual's ability to withstand treatment or their personal preferences simply based on chronological age. In this way true inequities in care can be eliminated.

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PERSPECTIVE

03 Improving Care for Older Cancer Patients in the NHS

Sean Duffy, Mike Birtwistle

NHS cancer services are improving. We are diagnosing more patients before their cancer has spread and providing more effective treatments delivered by expert teams. The experience reported by patients is increasingly positive and we know more about how to support people in living well after a diagnosis of cancer. There is much reason for encouragement and it is right that we celebrate the progress that has been made. Yet there is no room for complacency. Our outcomes are still not as good as in some national comparator countries, and the needs of cancer patients are changing. Worryingly, our outcomes appear to be poorer in the demographic group in which cancer will increase the most: older people. Cancer is predominantly a disease of older age and our population is ageing. More people will be diagnosed with cancer and their needs will be more complex.

Nearly two-thirds of cancer diagnoses occur in the over-65s and one-third in people aged 75 and over. In 2012, over 102,000 people over the age of 75 were diagnosed with cancer. Nearly 32,000 of them were over the age of 85.¹ By 2020 there will be nearly two million people aged 65 and over alive following a diagnosis of cancer. The growing impact of cancer in older people is reflected in the demand for cancer services. More than a quarter of all admitted episodes for cancer in England occur in the over-75s.² In the past decade, the increase in admissions in this group has far outstripped the increase observed for cancer patients of all ages.

Today's cancer services, however, were largely designed in the 1990s, a time when the average age of cancer patients was significantly younger. We are now faced with a choice: we can seek to perfect the existing model of cancer care or we can redesign cancer services to better meet the needs of older people. We firmly believe that we must take the latter approach, both so that we may achieve the best outcomes and make the best use of the resources available to us.

The needs of older people are not uniform, just as they are not for any group in society. The nature of malignancy, socioeconomic status, sex and ethnicity all play a role in shaping people's needs and outcomes. Equally, the needs of active older people in otherwise good health will be very different from those of people living with frailty and other health conditions. Yet there is evidence to suggest that older people appear to experience poorer outcomes. Older people are more likely to be diagnosed with cancer following an emergency admission, which diminishes their chances of long-term survival. They also experience poorer survival after diagnosis with a cancer that has already spread. Seeking to make earlier diagnosis in older people should be a major priority. We need to increase awareness of signs and symptoms of cancer, but we also need to increase motivation to seek help. Fear of cancer and the consequences of treatment may inhibit some people from seeking help. For older people, perhaps scarred by memories of old-fashioned cancer treatment received by friends or loved ones, this may be particularly potent. We need to better understand the factors that can lead to late diagnosis in older people.

We know that older patients are also less likely to receive active cancer treatment, be it surgery, radiotherapy or cancer drugs. In some cases, there will be good reasons for this. Frailty and other issues can reduce a person's ability to tolerate treatment and can result in an unacceptable impact

on quality of life. Older people may also opt not to receive treatment. Yet we know that treatment plays a vital role in improving outcomes. It is implausible that the reduction in treatment rates can be explained by patient comorbidities or patient preference alone, and factors that depend on professional attitudes are likely to play a part.

The social context for older people is relevant to the cancer care they might receive. Half of all people aged 75 and over live alone, and one in 10 people have less than monthly contact with friends, family and neighbours. Isolation can be particularly difficult when a person is receiving ongoing treatment.³ Furthermore, one in five people aged 75 and over state they find it very difficult to get to their local hospital.⁴ Caring responsibilities can also reduce the probability of people accepting treatment: over half a million people aged 65 and over have caring responsibilities that take up at least 20 h per week.⁵ It is necessary to assess whether a patient is physically and mentally able to tolerate treatment and whether a patient has the right social and care support in place to help him or her recover.

Overall, older people report a positive experience of cancer treatment and care. NHS services should be congratulated on their continued efforts to improve patient experience. In particular, older patients are more likely to report confidence in doctors and nurses and feel that they were treated with dignity and respect. Patient experience surveys nonetheless also identify areas for improvement. In particular, older people are less likely to have access to a clinical nurse specialist or report being given information on side effects of treatment. These issues are particularly concerning given that older people are more likely to have other health issues which will impact on their quality of life during and after treatment and which may necessitate enhanced support.

For older people with cancer who are near the end of their life, there are substantial variations in the length of time they spend in hospital, suggesting that some areas of the country are better than others in supporting people in the community. There is substantial scope to improve both the quality and efficiency of care in this respect.

Older people are less likely to have the chance to participate in cancer research, meaning that opportunities to develop the evidence base on how best to treat older people are missed. This not only potentially hinders their care but also compromises our ability to do the very best for future patients. As clinicians we should lament the absence of evidence on treatment in older people without doing everything we can to address it, including seeking to involve a greater number of older people in clinical trials and studies.

One estimate suggests that, if the UK matched US levels of survival for the over-75s, then 14,000 lives could be saved.⁶ Yet the outcomes we seek for older people should go beyond survival. Ensuring we treat older people safely and that we do all we can to protect their quality of life and help them recover from treatment as quickly and fully as possible are also important, as is doing what we can to ensure a positive experience of cancer care. There is also a strong economic argument for improving the way in which we support older people affected by cancer. There is nothing as inefficient as a treatment that is ineffective, so we must do more to ensure that the treatment we do provide delivers the outcomes that matter most to older people. Effective, tailored treatment can prevent recurrences or further spread of cancer and can also help to maintain a person's independence. Treatment for earlier stage cancer is less expensive than treatment for advanced disease.⁷ We must therefore do more to ensure that older people are diagnosed before their cancer has spread.

Age alone should never be a barrier to treatment, but asserting this is easier than removing the barriers that do exist. These barriers are not about funding or access to services: that would be illegal. They are, unfortunately, far more problematic to address than that. Any clinical decision

will be influenced by a range of factors in a clinician's life: his or her own attitudes, training, the service context, as well as previous experiences. On each of these issues, there is more that we can do to help our clinicians.

We should therefore do more to help clinicians assess a person's suitability for treatment, take steps to address factors that might limit the effectiveness of a treatment and, where necessary, tailor treatment options to suit a person's circumstances. Support needs to start with training, but we also need to support the existing workforce in managing older people more effectively. Furthermore, we must join up the medical aspects of care with the wider social factors that will impact on a person's cancer journey. To ignore either is to risk failing our patients when they need us the most. Of course, not all of these factors are in the direct control of cancer clinicians, but we need to look beyond the immediate issues we confront in our clinics and consider the whole picture.

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01 A Patient with Lung Cancer, Chronic Obstructive Pulmonary Disease, Hypertension and Dizziness

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Case history



A 71-year-old man presented with increasing shortness of breath, productive cough, lethargy, weight loss and haemoptysis. CT was suggestive of stage IV lung cancer (T4N3M1a), and bronchial biopsies confirmed squamous cell carcinoma. Past medical history included peripheral vascular disease, hypertension and chronic obstructive pulmonary disease (COPD). His medications included: salbutamol inhaler (as required), simvastatin, clopidogrel, bisoprolol, amlodipine and ramipril. He had been a lifelong smoker (60 pack-year history) and drank 24 units alcohol/week. He lived with his son in a first floor flat and mobilized independently with a stick.

A Barthel Index of activities of daily living (ADL) was used to assess his functional ability and revealed he needed assistance with bathing and using stairs. He also reported intermittent dizziness on standing and two falls (one associated with syncope) in the last 6 months. His lying BP was 130/90 mmHg, with a BP of 105/65 mmHg at 1 min, which improved to 120/75 mmHg at 3 min. His ECG showed sinus rhythm with a rate of 70 bpm and no ischaemic change. He was urgently referred to a falls clinic.

In view of metastatic non-small-cell lung carcinoma (NSCLC) he was offered palliative chemotherapy and opted for treatment to preserve his quality of life. Because of his respiratory and vascular comorbidities he received carboplatin AUC 5 and gemcitabine 1000 mg/m² with prophylactic antibiotics. He experienced severe nausea and required a dose reduction. He completed four cycles with no further complications and achieved partial response. Nine months later he progressed locally and proceeded to second-line chemotherapy with docetaxel 60 mg/m², with partial response. He progressed 4 months later with liver metastases and at this point his performance status (PS) had deteriorated significantly and he was offered best supportive care (BSC) by his community palliative team. He died at home approximately 18 months after the initial diagnosis.

What is the goal of cancer treatment for this patient?

What is the evidence base for treatment options in metastatic NSCLC?

What is the evidence base for treatment options in this patient?

How should this patient be optimized prior to starting cancer treatment?

What is the goal of cancer treatment for this patient?

The treatment aim in metastatic NSCLC is to control symptoms, preserve functional status and prolong survival. The patient wanted to stay at home with his son and was willing to accept additional support. With appropriate tailored chemotherapy he achieved 18 months' survival with a good quality of life.

What is the evidence base for treatment options in metastatic NSCLC?

Treatment decisions should be directed by a multidisciplinary cancer team and will depend on histology, molecular pathology, age, PS, comorbidities and patient preference. Four cycles of platinum-based doublet chemotherapy are recommended for patients with PS 0–2. In the presence of *EGFR* mutation, tyrosine kinase inhibitors (TKIs) should be offered as first-line agents in patients with PS 0–3. Second-line agents include taxanes and erlotinib. Enrolment into clinical trials should be considered. Patients with *ALK* rearrangement should be offered crizotinib. In patients unfit for systemic therapy, BSC should be offered.¹

What is the evidence base for treatment options in this patient?

NSCLC is a disease of older adults (median age at diagnosis 69 years; 47% diagnosed ≥ 70 years). As the population ages, an increasing number of patients with lung cancer are referred for treatment. Appropriate treatment depends on a comprehensive assessment to determine the patient's likelihood of dying from cancer rather than from other comorbidities, and also potential toxicity based on physiological function. Older patients can be categorized into those who are fit and will benefit from standard regimens, those who are vulnerable and need adjusted regimens, and those who are frail and should be offered BSC. This patient falls into the vulnerable category; therefore, carboplatin was used to avoid fluid overload and protect the kidneys, and doses were reduced and prophylactic antibiotics given in view of his COPD, as there is evidence that this decreases infection and mortality.

Randomized trials assessing first-line chemotherapy for older patients with metastatic NSCLC are limited (Table 1.1).^{2–9} The Elderly Lung Cancer Vinorelbine Italian Study (ELVIS)² established survival (21 vs 28 weeks; $p=0.03$) and symptomatic benefit with vinorelbine compared with BSC in patients with PS 0–2, but stopped early due to a low enrolment rate. Several trials have compared platinum doublets versus monotherapy. Quoix *et al.*⁷ demonstrated that carboplatin combined with paclitaxel was superior to single-agent gemcitabine or vinorelbine (overall survival [OS] 10.3 vs 6.2 months; $p<0.0001$) despite higher toxicity rates. Yet, in a recent trial,⁸ docetaxel combined with weekly cisplatin was inferior to docetaxel alone. In a series of age-based analyses of prospective trials, the feasibility and superiority of the doublets was established among the older subpopulation.

A comprehensive meta-analysis comparing doublets with single third-generation agents included 2510 older patients across 10 trials and demonstrated the superiority of platinum-based doublets in terms of 1 year survival ($p=0.009$) and responses ($p=0.000$), with worse haematological and neurotoxicity.⁹ To decrease toxicity, several trials have proposed non-platinum doublets versus monotherapy but have shown inconsistent results.

The TKIs gefitinib, erlotinib and afatinib are recommended in older patients either as first line in the presence of *EGFR* mutation or as second line in non-mutated patients (erlotinib), based on subgroup analysis of phase III trials. Older patients experience significantly more grade ≥ 3 toxicity with TKIs (35% vs 19%; $p<0.001$), including rash, fatigue and dehydration.

For vulnerable patients, either a single third-generation agent (gemcitabine, vinorelbine,

Table 1.1 Randomized trials assessing first-line chemotherapy in older patients with NSCLC.

Trial	N	Age (years)	Chemotherapy	RR	PFS	OS	p-value
Monotherapy							
ELVIS ²	161	>70	Vinorelbine vs BSC	19.7 vs 0	NR	6.9 vs 4.9	0.03
Kudoh <i>et al.</i> ³	182	>70	Vinorelbine vs docetaxel	9.9 vs 22.7	3.1 vs 5.5	9.9 vs 14.3	0.138
Non-platinum doublets							
MILES ⁴	698	>70	Vinorelbine vs gemcitabine vs vinorelbine + gemcitabine	18 vs 16 vs 21	4.2 vs 4.4 vs 4.4	8.4 vs 6.9 vs 7.0	0.93 0.65
SICOG ⁵	120	>70	Vinorelbine vs gemcitabine + vinorelbine	15 vs 22	NR	4.2 vs 6.8	
Comella <i>et al.</i> ⁶	264 (220) ^a	>70	Gemcitabine vs paclitaxel vs gemcitabine + vinorelbine vs gemcitabine + paclitaxel	18 vs 13 vs 23 vs 32	3.3 vs 3.7 vs 4.1 vs 4.5	5.1 vs 6.4 vs 9.7 vs 9.2	0.028
Platinum doublets							
Quoix <i>et al.</i> ⁷	451	>70	Gemcitabine or vinorelbine vs carboplatin + paclitaxel	10.2 vs 27.1	2.8 vs 6.0	6.2 vs 10.3	<0.0001
Abe <i>et al.</i> ⁸	276	>70	Docetaxel vs docetaxel + cisplatin	24.6 vs 34.4	4.4 vs 4.7	14.8 vs 13.3	NR
Meta-analysis							
Qi <i>et al.</i> ⁹	2510 (10 trials)	>70	Doublet vs single third-generation agent	1.54 95% CI 1.36–1.73 p=0.000	TTP HR 0.76 95% CI 0.60–0.96 p=0.022	HR 0.84 95% CI 0.71–1.00 p=0.053	0.053

^a220 patients were >70 years old.

NR, not reported; PFS, progression-free survival; TTP, time to progression.

taxane) or a weekly platinum doublet has been suggested despite the absence of evidence from phase III trials.

As the trials indicate that chemotherapy can improve survival when given to fit, older patients, standard platinum doublet chemotherapy should be discussed in patients with PS 0–1. Single-agent chemotherapy may be offered to vulnerable patients (Figure 1.1).^{10–14} It is important to recognize physiological changes associated with ageing in order to address toxicity-related issues early (Table 1.2). Early palliative care intervention is encouraged along with standard oncology care in all patients, as shown in a randomized trial.¹⁵

How should this patient be optimized prior to starting cancer treatment?

Falls and syncope

Falls associated with syncope should be thoroughly investigated to determine whether syncope is neural, orthostatic or cardiac in origin. All patients should have baseline ECG and postural BPs. If the diagnosis is uncertain, further investigations include 24 h ambulatory ECG for arrhythmias, tilt table testing encompassing carotid sinus massage (for carotid sinus and baroreceptor hypersensitivity), or an electroencephalogram.

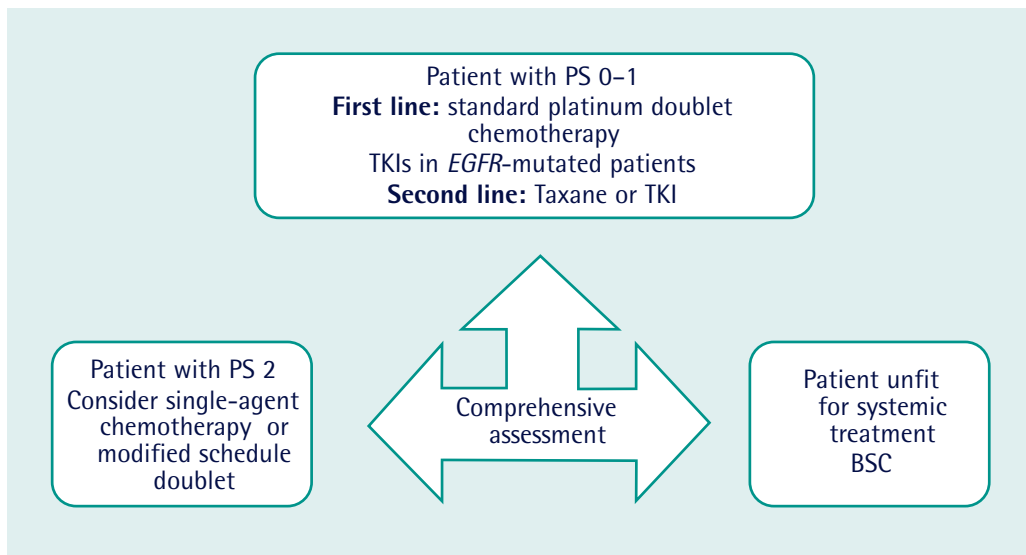


Figure 1.1 Recommendations for treatment in older patients with metastatic lung cancer.

Our patient was assessed in the falls clinic and found to have classical orthostatic hypotension (OH) with a systolic BP drop >20 mmHg.¹⁶ His normal ECG ruled out a cardiac cause. His OH was most likely drug-induced and his amlodipine and ramipril were stopped with good effect. He was advised to drink plenty of fluids. If these measures had not been successful, cessation of his beta-blocker, full-leg compression stockings, and pharmacological interventions with fludrocortisone or midodrine would be the next steps.

In view of the Barthel screening showing difficulty with ADL, an occupational therapist performed a home visit. Grab rails for the bath and handrails for the stairs (leading to the flat) were fitted, and decluttering of the property and removal of loose rugs to reduce the risk of falls were advised.

Although treatment of hypertension improves cardiovascular and cerebrovascular outcomes, it must be weighed against the side effects of medications and the life-limiting nature of the patient's cancer. Preventing further falls was the most important factor in this patient.

COPD, smoking and shortness of breath

Lung function tests 1 year previously were consistent with moderate COPD (Global Initiative for Chronic Obstructive Lung Disease, stage II [GOLD-2]), with an FEV₁ at 65% of predicted. His MRC dyspnoea scale was grade 4, having a significant impact on his walking ability.

A tiotropium inhaler (long-acting muscarinic antagonist) was added to salbutamol, as he was undertreated according to NICE guidelines¹⁷ (Figure 1.2). Tiotropium improves quality of life and reduces the number of chest infections. On assessment, the patient's inhaler technique was poor and was corrected. He was referred to the integrated respiratory team for follow-up.

Smoking cessation advice was given and nicotine replacement therapy offered, but he refused. There is no robust evidence to support smoking cessation in metastatic NSCLC. However, smoking after diagnosis of cancer increases the risk of a second primary tumour, cancer recurrence and treatment complications.¹⁸

Table 1.2 Physiological changes associated with ageing and how they should be addressed.

Reduced glomerular filtration rate	<ul style="list-style-type: none"> • Ensure hydration • Caution with diuretics • Avoid nephrotoxic drugs • Choose carboplatin over cisplatin and base dose on EDTA • Monitor renal function with nephrotoxic agents (platinum, pemetrexed)
Impaired fluid/electrolyte haemostasis	<ul style="list-style-type: none"> • Risk of fluid overload • Monitor prehydration • Monitor electrolytes in gastrointestinal toxicity
Impaired gastrointestinal function	<ul style="list-style-type: none"> • Supply mouthwashes • Caution with TKI-related diarrhoea • Constipation: consider early introduction of laxatives • Caution with antiemetics
Decrease in the activity of the cytochrome P450 system Polypharmacy Warfarin	<ul style="list-style-type: none"> • TKIs/taxanes may present increased toxicity • Ensure no drug interaction • Review indication for medications • Change to low-molecular-weight heparin
Coexisting peripheral neuropathy	<ul style="list-style-type: none"> • Monitor carefully with neurotoxic chemotherapy (taxanes, vinca alkaloids, platinum) and apply dose reduction if needed
Decreased cellularity in bone marrow	<ul style="list-style-type: none"> • Consider prophylactic growth colony-stimulating factor • Mid-cycle nadir blood counts • Anaemia should be treated aggressively • Folic acid and vitamin B₁₂ should be administered with pemetrexed • Prophylactic antibiotics
Use of indwelling catheter	<ul style="list-style-type: none"> • Remove if possible (if needed discuss with urology or continence adviser) • Consider prophylactic antibiotics
Impaired memory	<ul style="list-style-type: none"> • Consider written instructions and contact numbers

Other considerations

Renal function. This is likely to be affected by chemotherapy. Nausea and vomiting may lead to dehydration and acute kidney injury. Discontinuation of ACE inhibitors (in this case, ramipril) should be considered during chemotherapy to reduce the risk of acute kidney injury. Dehydration will worsen OH.

B vitamins. This patient drinks more alcohol than the recommended limit, which can also increase OH. He is at risk of vitamin deficiencies (B₁₂, thiamine and folate), which can lead to neurological complications. Levels should be measured and corrected. He should be advised to reduce his alcohol intake. Certain chemotherapy agents can cause peripheral neuropathies and worsen symptoms.

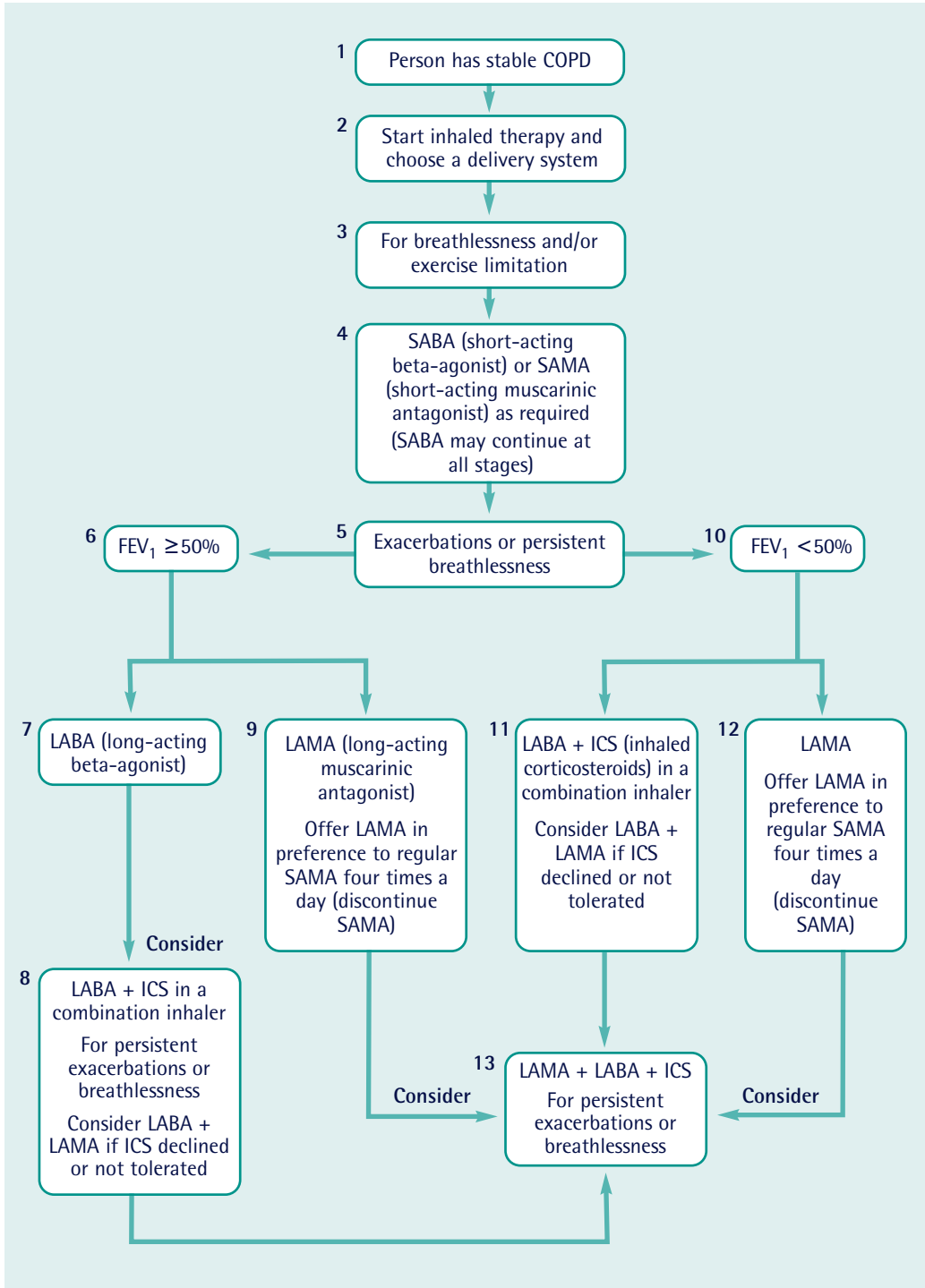


Figure 1.2 NICE pathway for inhaled therapy in COPD.¹⁹

Conclusion and learning points



- Older patients with metastatic lung cancer should not be excluded from palliative systemic therapy options on the basis of age alone.
- Treatment decisions should be based on a comprehensive assessment.
- Extra care should be applied to toxicity monitoring, and treatment modifications may be required.
- Falls associated with syncope must be investigated and managed in a multidisciplinary falls clinic.
- ECG and lying and standing BP can be measured in oncology clinics, and if OH is present with an unremarkable ECG first-line treatment of stopping antihypertensives and increasing fluid intake may be instituted.
- Symptomatic COPD can be optimized with additional inhalers and checking inhaler technique.

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CASE STUDY

02 Colorectal Cancer in a Patient with an Aortic Abdominal Aneurysm, Peripheral Vascular Disease and Poor Nutritional Status

Dimitra Repana, David Shipway, Paul Ross

Case history



A 75-year-old man presented to his GP complaining of fatigue, progressive weight loss of 12 kg and low mood. His past medical history consisted of peripheral vascular disease (PVD) presenting with calf claudication and hypertension diagnosed 20 years previously. He was an ex-smoker with a history of 40 pack-years and drank 4–6 units of alcohol per week. He was a retired librarian who lived alone after his wife died 2 years previously.

His medications included aspirin 75 mg/day, ramipril 10 mg/day, amlodipine 10 mg/day, bendroflumethiazide 2.5 mg/day, simvastatin 20 mg/day and naftidrofuryl oxalate 200 mg three times daily.

His performance status was 2 and his BMI was 21.2 kg/m² (height 175 cm, weight 65 kg). Physical examination revealed a palpable mass in the left lower abdomen. His score on the Patient Health Questionnaire (PHQ-9) was 10 (moderate depression).

Further investigations revealed microcytic anaemia with haemoglobin 94 g/l and low iron levels 6 µmol/l. A colonoscopy was organized and a partially obstructing tumour was seen in the sigmoid. Biopsies confirmed a moderately differentiated adenocarcinoma of the colon. Staging was completed with a CT scan of chest, abdomen and pelvis, which showed, apart from the colonic tumour, pericolic lymphadenopathy and a 7.5 cm abdominal aortic aneurysm (AAA).

The patient was started on mirtazapine for his depression and was assessed by a dietitian for his weight loss. Nutritional supplements were initiated in addition to carer support at home with meal preparation. After discussion with the vascular team it was decided that AAA repair with endoscopic repair of abdominal aortic aneurysm (EVAR) should proceed. A colonic stent was inserted and preoperative intravenous iron was given to optimize his haemoglobin. EVAR was performed without complications. During admission, sodium was found to be low at 124 mmol/l and bendroflumethiazide was stopped. A laparoscopic anterior resection of his sigmoid tumour was performed 6 weeks afterwards. Histology showed a pT3N2 (6/18 lymph nodes) M0 adenocarcinoma of the sigmoid colon with lymphovascular invasion.

The patient was referred to the oncology team to discuss adjuvant chemotherapy after his surgery. Both options of single-agent capecitabine and doublet

chemotherapy with fluoropyrimidine and oxaliplatin were discussed. After considering potential benefit and side effects, single-agent capecitabine was considered more appropriate.

What is the optimal management of his anaemia, weight loss and depression?

What are the usual causes of hyponatraemia in older people?

How do AAA and PVD affect his management?

What are the evidence-based data regarding surgical options in this population and what is the role of stenting used as a bridge to surgery?

What is the evidence for adjuvant chemotherapy?

What is the optimal management of his anaemia, weight loss and depression?

Preoperative anaemia has been associated with increased 30 day mortality and morbidity in patients undergoing major surgery.¹ Iron deficiency anaemia in patients with colorectal cancer is common, but further causes of anaemia in the older population should also be excluded² (Figure 2.1). Iron replacement with intravenous iron is safe and effective in the perioperative setting. It results in more rapid optimization of body iron stores, compared with enteric replacement, and may be better tolerated than oral preparations especially in patients vulnerable to constipation or obstructive symptoms³ (Figure 2.2).

Pre-existing depression has been found to be a significant risk factor for complications and prolonged recovery from colorectal cancer surgery.⁴ Antidepressants are chosen based on patient characteristics and toxicity profile.⁵ Selective serotonin reuptake inhibitors (SSRIs) have been associated with increased bleeding risk.^{6,7} Mirtazapine has been shown to be safer in this context and has a faster result in 2 weeks compared with SSRIs (OR 1.57, 95% CI 1.30–1.88; $p < 0.00001$). It is also associated with improved appetite and weight gain.^{8,9}

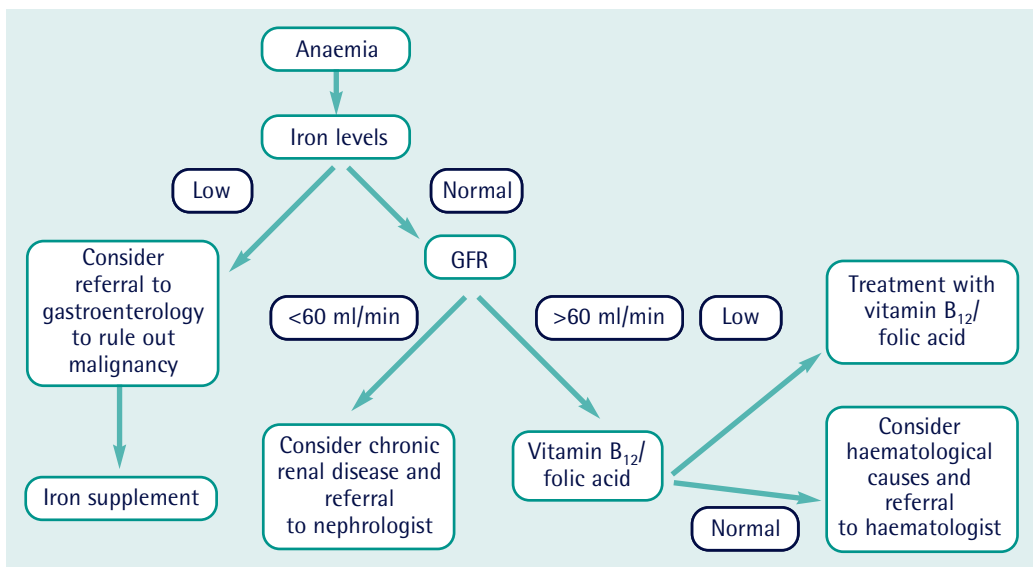


Figure 2.1 Algorithm for evaluation of anaemia in older patients (adapted from Goodnough and Schrier²). GFR, glomerular filtration rate.

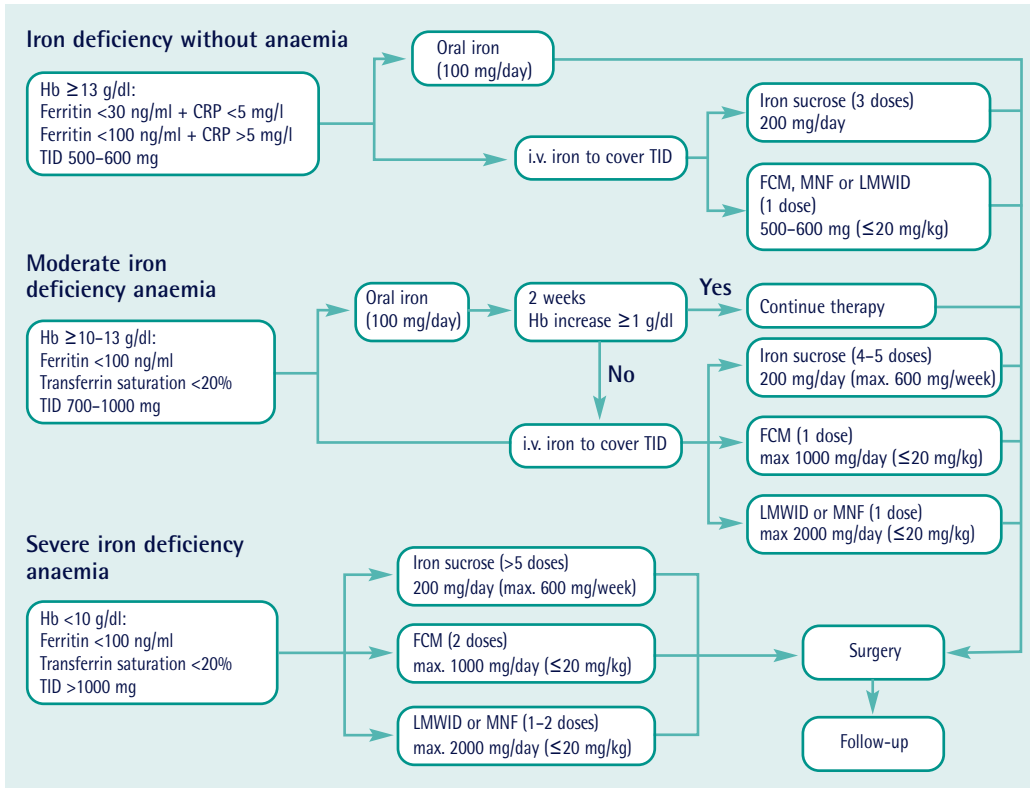


Figure 2.2 Algorithm for correction of anaemia (adapted from Muñoz *et al.*³). CRP, C-reactive protein; FCM, ferric caboxymaltose; LMWID, low molecular weight iron dextran; MNF, iron isomatolside-100; TID, total iron deficiency.

Weight loss in older people can be multifactorial and in this case, apart from cancer, depression and isolation contribute. Poor nutrition has been associated with worse outcomes for patients undergoing cancer surgery.¹⁰ Various screening tools are used for initial assessment. Further management is determined according to severity of weight loss and circumstances. This includes assistance with feeding or shopping, especially for isolated patients, nutritional supplements, appetite stimulants, and enteral and parenteral feeding. For surgical candidates who are at risk of malnutrition (Table 2.1), or who are already malnourished and oral intake is inadequate or unsafe, an enteral tube should be considered if they have a functional and accessible gastrointestinal tract. In case of a non-functional, perforated or inaccessible gastrointestinal tract, parenteral nutrition is indicated.¹¹

Table 2.1 Definitions of malnutrition and risk of malnutrition.¹¹

Malnutrition	<ul style="list-style-type: none"> • BMI < 18.5 kg/m² • Unintentional weight loss $> 10\%$ within last 3–6 months • BMI < 20 kg/m² and unintentional weight loss $> 5\%$ within last 3–6 months
Risk of malnutrition	<ul style="list-style-type: none"> • Has eaten little or nothing in last 5 days and/or is likely to eat little or nothing in the next 5 days or longer • Poor absorption and/or high nutritional losses and/or high nutritional needs

What are the usual causes of hyponatraemia in older people?

Hyponatraemia is the most common electrolyte disorder in older patients and is observed in more than 20% of geriatric inpatients.¹² It is associated with impaired cognition, higher risk of osteoporosis, falls and fractures, prolonged admission and readmission to hospital and increased mortality.¹³ Mild hyponatraemia is usually asymptomatic; neurological symptoms develop depending on severity and onset and include headaches, malaise, nausea and vomiting, confusion, cramps, seizures, delirium, coma, neurogenic pulmonary oedema and brain oedema with fatal herniation.¹⁴

Hyponatraemia can often be multifactorial: the usual causes are shown in Table 2.2.¹⁵ Several medications can cause low sodium levels, and a thorough medication history should be obtained. In our patient, hyponatraemia was attributed to the combination of a thiazide diuretic with an antidepressant.

Table 2.2 Major causes of hyponatraemia (adapted from Sterns¹⁵).

Disorders in which ADH levels are elevated

Effective circulating volume depletion

- True volume depletion
- Heart failure
- Cirrhosis
- Thiazide diuretics

Syndrome of inappropriate ADH secretion, including reset osmostat pattern

Hormonal changes

- Adrenal insufficiency
- Hypothyroidism
- Pregnancy

Disorders in which ADH levels may be appropriately suppressed

Advanced renal failure

Primary polydipsia

Beer drinker's potomania

Hyponatraemia with normal or elevated plasma osmolality

High plasma osmolality (effective osmols)

- Hyperglycaemia
- Mannitol

High plasma osmolality (ineffective osmols)

- Renal failure
- Alcohol intoxication with an elevated serum alcohol concentration

Normal plasma osmolality

- Pseudohyponatraemia (laboratory artefact)
 - High triglycerides
 - Cholestatic and obstructive jaundice (lipoprotein X)
 - Multiple myeloma
- Absorption of irrigant solutions
 - Glycine
 - Sorbitol
 - Mannitol

ADH, antidiuretic hormone.

How do AAA and PVD affect his management?

For AAA greater than 5.5 cm there is at least a 20% risk of rupture at 1 year, which increases exponentially with diameter; thus, surgical intervention should be considered¹⁶ (Figure 2.3). EVAR is a major advance in vascular surgery, since it is associated with reduced perioperative mortality.¹⁷ Data support the use of EVAR in older patients who meet the anatomical criteria for the procedure.¹⁸

Age, smoking, diabetes, hypertension and hypercholesterolaemia are well-established risk factors for PVD. Undiagnosed ischaemic heart disease is an underlying factor in 40–60% of patients with PVD,¹⁹ and a meticulous history of cardiac and respiratory symptoms should be sought, along with routine preoperative ECG. Patients with vascular disease have a high prevalence of undiagnosed cognitive impairment that can affect up to 60% of those presenting for vascular surgery; these patients are at high risk of perioperative delirium, which may influence the choice of anaesthetic technique.²⁰

PVD is graded according to severity, and mild claudication improves with medical treatment and increased exercise. In this case it should not influence decisions regarding further management.²¹ Secondary prevention medications are likely to be in use, and ACE inhibitors should be withheld on the morning of surgery. Antiplatelet agents may also need to be discontinued depending on the nature of the surgery undertaken, although in the context of coexisting ischaemic heart disease this may need to be with caution.

What are the evidence-based data regarding surgical options in this population and what is the role of stenting used as a bridge to surgery?

Comprehensive Geriatric Assessment (CGA) in the perioperative setting can identify risks that may increase mortality and help the multidisciplinary team of surgeons and oncologists towards better and safer treatment decisions for older patients with cancer.²²

Data support a laparoscopic approach over open surgery in this age group.²³ A recently published meta-analysis including more than 70,000 older patients showed no difference in survival outcomes (OR 0.89, 95% CI 0.45–0.68; $p < 0.01$) but improved postoperative complications (OR 0.55, 95% CI 0.48–0.63; $p < 0.01$) and mortality (OR 0.55, 95% CI 0.45–0.68; $p < 0.01$).²³

Colonic stenting versus emergency surgery for obstructing left-sided tumours has been

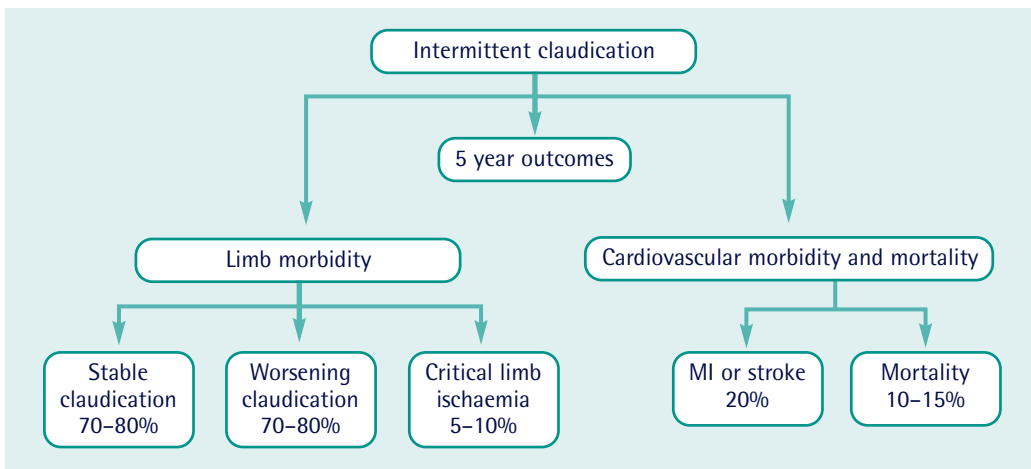


Figure 2.3 Natural history of PVD (adapted from Conte *et al.*²¹). MI, myocardial infarction.

associated with reduced stoma formation and higher primary anastomosis.²⁴ Owing to lack of randomized trials, few data are available for the use of colonic stents as a bridge to elective surgery. It may be reasonable to use stenting whilst medical optimization is achieved.²⁵

What is the evidence for adjuvant chemotherapy?

Between 2009 and 2011, 43% of all patients diagnosed with colorectal cancer in the UK were >75 years old.²⁶ Management of older patients demands an individualized approach due to significant heterogeneity in this group. Holistic assessment allows consideration of physiological rather than chronological age, comorbidities and social issues.²⁷

There are concerns about oncological undertreatment of older patients,²⁷ and age has been observed as a major reason for not offering adjuvant treatment.²⁸

Adjuvant chemotherapy following colorectal cancer surgery improves disease-free survival and overall survival (OS); therefore, it should be discussed with patients with node-positive tumours and selected patients with node-negative tumours with other adverse prognostic features.²⁹ The discussion will need to consider recurrence risk, potential survival advantage and risks of chemotherapy. Subgroup analyses of both the Multicenter International Study of Oxaliplatin/5-Fluorouracil/Leucovorin in the Adjuvant Treatment of Colon Cancer Trial (MOSAIC)³⁰ and the National Surgical Adjuvant Breast and Bowel Project (NSABP C-07)³¹ questioned the benefit of adding oxaliplatin to fluorouracil-based chemotherapy for patients above 70 years of age. Conflicting results were reported in the Study of Bevacizumab Alone or Combined with Capecitabine and Oxaliplatin as Support Therapy in Metastatic Colorectal Cancer Patients (XELOXA), where adding oxaliplatin to capecitabine chemotherapy in patients with colon cancer was found to be beneficial for all age groups compared with fluoropyrimidines.³² The ACCENT database, which used individual patient data and included all previous studies plus four further trials, suggested that there may be a disease-free survival benefit for patients >70 years but not an OS benefit.³³ Another recently published pooled analysis supported the benefit of oxaliplatin in patients over 70, which was maintained even after adjustment for comorbidities.³⁴ As randomized controlled trials are lacking in this specific age group, and data from subgroup analyses from previous studies are conflicting, adding oxaliplatin appears reasonable for fit patients between 70 and 75 years of age. Online tools such as Adjuvant! Online (www.adjuvantonline.com) can help shared decision making and estimate the risk of recurrence, life expectancy and potential benefit of chemotherapy.

Conclusion and learning points



- Optimization of haemoglobin prior to surgery with intravenous iron is both safe and effective. It may be better tolerated in patients with colorectal cancer, who are vulnerable to symptoms of gastrointestinal upset associated with oral iron preparation. Other contributing causes of anaemia should also be excluded.
- Antidepressant treatment with SSRIs has been associated with increased bleeding risk and should be avoided. Mirtazapine is an excellent alternative, as it offers appetite stimulation, which may promote secondary nutritional optimization.
- Dietetic review should be carried out to assess nutritional status and habits, with further management according to severity of weight loss.
- Older patients often have chronic low sodium levels associated with complications and mortality.

- CGA and optimization throughout the surgical pathway reduce complications and inpatient length of stay.
- EVAR is safe and provides advantages compared with open surgery for AAA.
- Laparoscopic surgery is preferred in older patients, since it is associated with fewer complications and mortality.
- Referral to the oncology team for discussion of risks and benefits of adjuvant chemotherapy for all patients who are fit for treatment should always be considered.

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