Prehabilitation and Rehabilitation for patients with lung cancer

Where are we today?

A review of the published literature was completed in PubMed and Medline for English language articles between January 2000 and March 2022. MeSH headings were used to create the search strategy included: lung cancer, lung tumour, lung carcinoma, lung neoplasm, prehabilitation, rehabilitation, diet, exercise, activity, nutrition, diet, smoking cessation, psychological support and well-being. The results of the review were supplemented with other pertinent sources such as relevant websites.

Introduction

Lung cancer is the third most common type of cancer in the United Kingdom (UK) with around 48,500 new cases diagnosed a year [1]. The incidence of lung cancer is predicted to increase over the next 10-20 years (about 15,000 more cases per year in 2035) [2] and the number of deaths attributed to lung cancer will continue to increase though more people will live with possible consequences of treatment as a result of increased survival rates [2].

Lung cancer is more common in the older population with an increased presence of comorbidities [3]; 54% presenting with three or more [4]. Socio economic disparities and deprivation levels also result in increased lung cancer diagnosis when compared to the average population [5]. It has been suggested that this deprivation gap has increased during the recent global pandemic and it is anticipated that the number of future lung cancer diagnoses may be higher than originally predicted [6].

Optimising the patients' physical and mental health, mitigating the effects of comorbidities prior to, during and after treatment, may increase the quality of life (QoL) and increase the survival of lung cancer patients [7]. By increasing the mental/physical fitness of lung cancer patients and providing support for stopping smoking, increasing activity, maximising dietary health, and preserving mental wellbeing, it is anticipated that there will be an improvement in the wellbeing and potentially survival of these patients.

Therefore, there is an urgent need to improve the general health of lung cancer patients before, during and after treatment to improve patient's quality of life and overall survival.

Prehabilitation, Peri-rehabilitation or post-rehabilitation?

The concept of prehabilitation is not new [8,9]. The use of prehabilitation programmes have been routinely used in orthopaedic surgery for many years resulting in decreased surgical complication rates, shorter hospital stays and quicker return to normal activity [10-12]. The translation of prehabilitation into cancer pathways is becoming more frequent. Embedding behavioural lifestyle changes and psychological support or signposting patients to appropriate services are becoming increasingly common [13].

Recent implementation of prehabilitation into the surgical lung cancer pathway has become more prevalent [14]. For example, intense programmes of exercise prior to surgery have been developed to reduce the side effects of the surgical insult [15,16]. However, timescales to prepare patients for surgery are short as there is the need to treat the patient as soon as possible and, in the NHS, the additional finite window of opportunity between diagnosis and surgical intervention to meet the 31 and/or 62-day lung cancer pathway. In addition, within this short perioperative timeframe, several diagnostic and physiological tests need to be performed. Thus, delivering a prehabilitation programme remains a challenge [17,18].

The practical implications of adhering to treatment targets mean that the opportunity to provide prehabilitation are challenging and that the realistic deployment of support to lung cancer patients sits within the timeframe including pre during and post treatment: prehabilitation/rehabilitation. One RCT, the PROLUCA study [19], found that it was impractical to implement a perioperative exercise intervention due to the short time between referral and surgery [16].

Patients undergoing radiotherapy have not traditionally been included in the offer of support interventions. Radiotherapy technology and practice have advanced significantly in recent years, increasing the chance that patients can be cured of lung cancer and more patients are surviving their lung cancer but die due to other existing medical conditions [20]. Curative radiotherapy is not a “one off” treatment with side effects occurring during (up to six and a half weeks) and after treatment, which allows the interventions to be tailored around the whole treatment pathway from the decision to treat (pre), during (peri) and after (post) the radiotherapy treatment.

There is benefit in providing prehabilitation [21] but the lack of large clinical trials does not provide definitive evidence on who should be included, what combination of interventions should be included, where and when the interventions should occur.

Support interventions

A number of lifestyle behaviours have been acknowledged to provide benefit to the well-being of individuals. Published evidence describing potential support mechanisms for lung cancer patients describe a range of physical and mental support for lung cancer patients [19,22-27].

There is no consensus on what exactly should be included in prehabilitation programmes for lung cancer patients or when it should be performed. Published prehabilitation programmes include: a range of aerobic and non-aerobic exercise, support on stopping smoking, psychological support, pulmonary exercises and improving diet [14,28-32]. A summary of support interventions and standard of care within the lung cancer patient pathway and their effects on patients' quality of life can be seen in Figure 1.

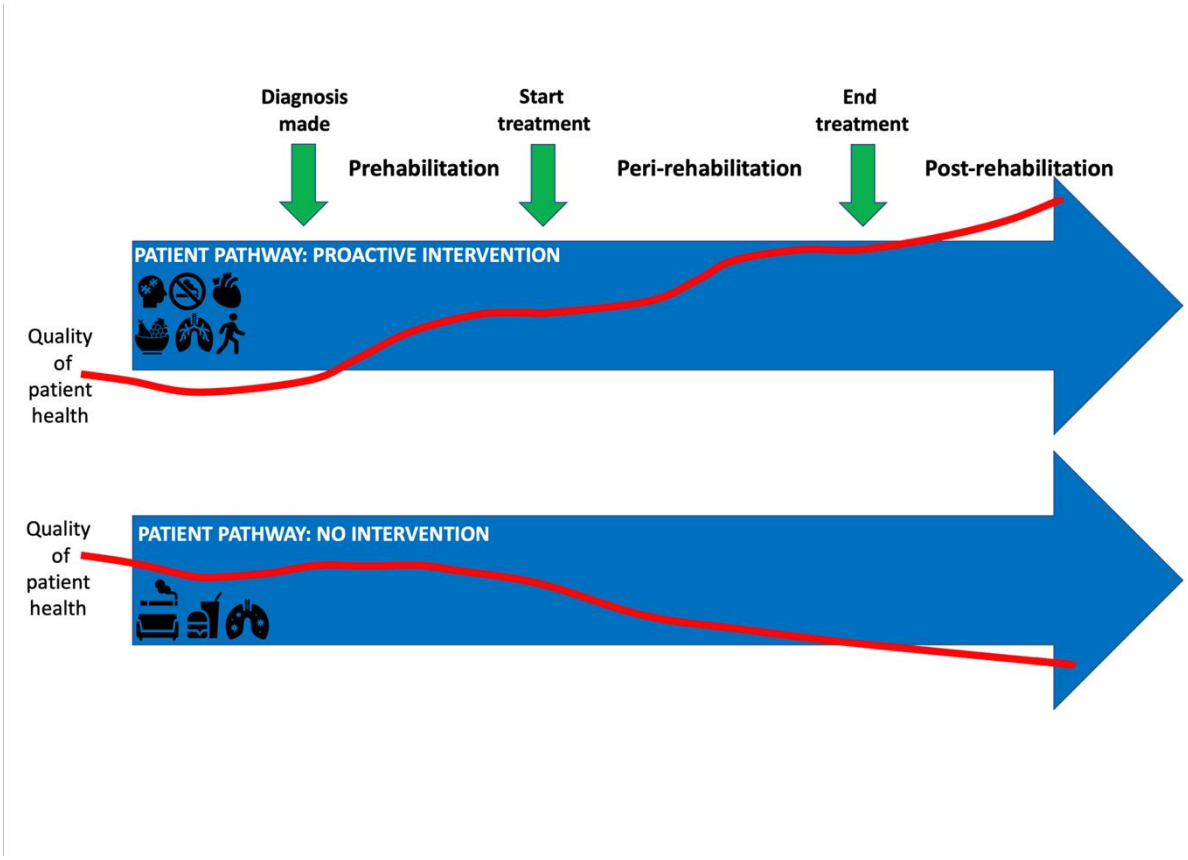

Figure 1 A summary of support interventions and standard of care within the lung cancer patient pathway and their effects on patients' quality of life

Affirmation of the interventions behind the prehabilitation for patients undergoing treatment for lung cancer study have been confirmed in two major strategic documents:

1. At their 2018 Cancer Conference, The National Cancer Research Institute (NCRI) announced their top ten research priorities with diet and exercise specifically mentioned in relationship to improving recovery from treatment, restoring health and improving quality of life [33].
2. The National Health Service (NHS) long term plan identified lung cancer and pulmonary rehabilitation as key areas of interest and investment [34].

Exercise

Studies have looked at the effect of exercise in patients with lung cancer with growing support for prescribing exercise before, during and after treatment [35-38]. Increasing patients physical activity to recommended levels is safe and effective at improving mental and

physical health (e.g. cancer related fatigue) [7] and decreasing the risk of secondary cancers. However, changing the behaviours of those patients who do not currently participate in exercise is a challenge and a programme of activity that is acceptable by the individual is required. Nomenclature may be seen as a barrier to promoting exercise to patients regarding exercise. *'Exercise'* may bring up connotations of high intensity exercise requiring vigorous effort, e.g., circuit training in a gym, which can be a daunting prospect for lung cancer patients. However, the aim is to gradually increase the activity levels of patients using low-impact exercises such as walking or chair-based routines. If patients do entertain the idea of attending gyms, the additional barriers of cost and travel may preclude patients from undertaking a proposed exercise programme. Funding for patients to attend council supported gyms has been secured by some institutions [39] but this is not available throughout the country.

Dietary advice

Malnutrition is common in patients with lung cancer and is associated with a negative prognosis [40-44]. Often the level of malnutrition increases over the period of treatment time. Unsal et al found that 31% of patients referred to radiotherapy were malnourished which increased to 43% at the end of radiotherapy treatment [45]. Patients who are well nourished and eat a balanced diet are stronger and have better tolerances to treatment side effects [46]. The provision of regular dietetic support during treatment will enable a proactive assessment and management rather than being reactive. Personalised nutritional counselling has been shown to improve nutritional intake and QoL [40].

Smoking cessation

Smoking cessation has been identified as the most important lifestyle change, a patient can make to maximise the effect of treatment and to improve their quality of life [47-51].

Evidence shows that stopping smoking increases the performance status and survival rate in patients [48-50,52-54]. Smoking impairs healing, reduces efficacy of treatments and increases the risk of recurrence of lung cancer [55]. However, despite being given a diagnosis of a cancer which is directly attributed to smoking, approximately 50 % of patients continue to smoke

after diagnosis [55]; 43% of patients were current smokers in an audit of 206 Yorkshire lung cancer patients 2016 [56]. National and local campaigns have been run to highlight the importance of stopping smoking and the potential health benefits [49,57,58]

The NHS actively encourages smoke free environments and provides mechanisms to support individuals quitting smoking [59]. Nonetheless cessation rates remain low [60,61].

Psychological support

As with any life changing diagnosis, patients will struggle with mental well-being. Lung cancer patients with a smoking history may suffer more, because of a perceived guilt and blame relating to their smoking. As previously mentioned, lung cancer patients often come from more deprived backgrounds, where socioeconomic situations compound and exacerbate poor mental health. This compounded with a global increase of mental health issues consequences from the global COVID-19 pandemic possibly from delayed diagnosis and isolation , have resulted in the increase of complex health requirements of the cancer patient [62].

Pulmonary rehabilitation and medical optimisation

In addition to general fitness, pulmonary fitness is an important factor in patients with lung cancer [63]. There is little published research evaluating the impact of optimising pulmonary function before radiotherapy. Rehabilitation programmes for patients with Chronic Obstructed Pulmonary Disease (COPD) are available, with a fast-track community-based service for surgical candidates [64]. However, a focus on the primary diagnosis of lung cancer rather than other comorbidities such as COPD, means that patients are not routinely referred to these services.

Cardiac health

Cardio oncology is an emergent subspeciality in cancer treatment. Living with and beyond cancer and potential cardiac toxicities due to new treatments such as immunotherapy has increased an interest cardio vascular disease and cancer [65].

Lung cancer patients commonly co-present with cardiac vascular disease (CVD); the determinants of cause are similar; smoking history, sedentary lifestyle, and poor diet [66]. Occult cardiac disease is also commonly present as shown in a large retrospective audit of lung cancer patients treated with radical radiotherapy. In this single centre study >50% of patients have a QRISK2 predicted 10-year cardiovascular risk of >20% [67].

Treatment of lung cancer (surgical and radiotherapy) can be damaging to the heart and modern radiotherapy techniques have modified to spare crucial cardiac structures. There is increasing evidence of the potential early effects of radiotherapy damage to heart.

Radiotherapy is known to cause radiation-induced heart disease many years after treatment in patients treated for breast cancer and lymphoma. However, there is increasing dosimetric evidence of the effects of radiotherapy damage to heart being linked to worse overall survival [68,69]. In addition, a large UK retrospective data analysis of > 100000 cancer patient with >500000 match controls showed an increased risk of coronary artery disease post cancer treatments, and with radiotherapy alone and with combined chemotherapy and radiotherapy there was an increased risk of arrhythmias and heart failure/cardiomyopathy post treatment compared to the control population [70]. The RAPID- RT study, a large-scale research programme funded by the National Institute for Health Research, will show how the use of rapid learning techniques on real-world data within a national learning healthcare system could provide evidence for a heart dose limit [71]. Early cardio-oncology input strives to provide patients with options to mitigate the side effects of the lung cancer intervention and rehabilitation post treatment [72] and therefore should be considered as a key part of rehabilitation/patient optimisation alongside ongoing trials in cardiac dose avoidance.

Where?

The Covid-19 pandemic has affected healthcare in the United Kingdom since 2020. On March 23rd 2020, the government of the United Kingdom put the country into lockdown and enforced measures to attempt to reduce the spread of the virus.

The lockdown and subsequent public health measures have affected everyone and all areas of society. The introduction of social distancing has affected the way we deliver healthcare

and the way we work. It is no longer possible to hold face to face meetings with colleagues, there is a need to reduce the number of people in confined spaces to ensure that an appropriate distance between individuals can be maintained and the number of hospital-based patient appointments has been minimised.

The mechanisms for the delivery of support for our patients must be designed to provide an effective service but to also maintain the health of our staff and patients. Virtual clinics and light touch signposting may replace group activities and additional hospital visits.

When?

Patients with a recent diagnosis of lung cancer have to come to terms with the possible repercussions of the diagnosis and treatment. The mental stress of comprehending the diagnosis and treatment plan may prevent patients from having the 'head space' to engage with possible modifications in their lifestyle. Commencing treatment may preclude patients from agreeing to consider or implement, modifying any health style changes.

Discussion

No one disputes the benefits the optimisation of the health of our lung cancer patients whilst having treatment. The interventions that are commonly implemented are not novel, they are tried and tested lifestyle behavioural modifications.

The gap in the evidence is the how, what and when to introduce a patient specific "tailored" intervention package. We also need detailed consideration of what resources are needed within a department and community to provide this support.

Lung cancer patients are often elderly, ex or current smokers and have co-existing medical comorbidities. They may not have led a healthy lifestyle prior to diagnosis, do not participate in exercise and have limited access to technology. Their family and friends may also share these lifestyle choices, which may hamper the individual if they want to engage with a rehabilitation scheme whilst undergoing treatment for lung cancer [73-75].

The health service also faces challenges: where costs are increasing, community services are overwhelmed, the current health service is working at, or beyond capacity and is still

recovering from the effects of the global pandemic. Thus, careful consideration and stratification is required to identify where the best investment of resources will provide the best outcomes [76]. It would appear sensible to offer all patients access to bespoke rehabilitation packages though this may not be achievable within current NHS constraints and in the face of rising inequalities. In addition, there is the lack of evidence and consensus opinion to determine which patients would benefit the most.

Key questions are:

- Should we enlist all patients, regardless of their performance status (PS) into a rehabilitation programme? An alternative would be to target those patients with good PS with the aim to maintain this during and after treatment or focus on poor PS patient with the aim to enable them to receive treatment.
- Should we just look at curable patients whether they be surgical or radical radiotherapy candidates or expand to all stages of diseases? In the era of targeted agents and immunotherapy with median overall survival measured in years rather than months that a rehabilitation programme during palliative systemic therapy would have the potential to improve quality and quantity of life both the curable and palliative setting.
- Should all patients be offered a low-cost general intervention, or should a more selective intensive service be provided to those who anecdotally would be seen to probably benefit more?

The published evidence supports increasing patient activity, reducing and stopping smoking, the provision of dietetic support, psychological assistance; the continued debate is how, where, and when.

Some patients may have limited capacity to engage with supportive programmes at the time of diagnosis. The enormity of the possible consequences of a life changing diagnosis, the understanding of the proposed treatment pathway and possible side effects, are too much for some patients, and prevent them from engaging in any dialogue. Is it because they are convinced that their diagnosis has one outcome, death, and see it as futile to consider

changing lifelong habits though they may be beneficial to them after they have completed treatment?

The practicalities of trying to incorporate additional appointment visits with appropriate staff groups between diagnosis and surgical intervention are challenging, and often unachievable, for the treating organisation to meet local and national treatment targets.

The timing of offering the support to patients may influence the uptake from our patients. We may see an increased engagement if the possible interventions were offered at the right time for that patient, which may be after the diagnosis and initial treatment has finished.

A further challenge to consider is the persisting nihilistic attitudes to a lung cancer diagnosis which may deter patients and non-cancer clinicians to actively engage in a rehabilitation programme and convince them that there is benefit to changing their behaviours to improve their quality-of-life post treatment.

The *brief intervention* is a possible way to reach all patients providing them with basic information about the benefits of modifying lifestyle behaviours but there is no continued support and adherence levels may be low. Health Education England describe and support 'Making Every Contact Count', an ethos of maximising the time spent with a healthcare professional to improve the health of every patient [77]. The use of this time to provide a brief intervention, signposting the patients to appropriate resources could be all that is needed to change a patient's behaviour.

The *'Small steps to feeling good'* website states 'some exercise is better than none' and provides a continuum of exercise programmes that can be performed by anyone [78]. The simple instructions provide patients with instructions to safely perform a range of core strength exercises.

For other patients 5K Your Way host monthly events throughout the country which are aligned to Park Runs. These events, open to anyone, provide a community-based event to allow cancer patients to increase their activity. It may not just be the increased activity

event that is attractive to patients, but a larger holistic support network that comes with the event.

A more formalised mechanism of embedding rehabilitation into the patient's pathway is being researched at Leeds Teaching Hospitals NHS Trust. The PREHABS research project, funded by Yorkshire Cancer Research, is a feasibility study evaluating the optimal way to implement a support package for lung cancer patients undergoing radiotherapy. The interventions have been delivered into the standard of care pathway, meaning there are no additional visits for patients. Therapeutic radiographic staff have been upskilled to provide motivational behaviour support and trained as smoking cessation practitioners. This allows for a bespoke service to be provided to patients without additional visits and a mechanism to measure adherence and provide continued support.

Other centres have provided community based rehabilitation resources, to which patients are signposted to whilst having treatment [39]. This maybe more cost effective to the institution providing the healthcare, but whether this approach has a similar uptake rate and adherence levels to more "hands-on" approaches is not known.

There is a growing resource repository growing, sharing examples of good practice and exemplars of prehabilitation/rehabilitation. These are openly available if you know where to look. Some are designed for clinicians, some for patients and some for both.

Macmillan Cancer Support have also identified that there is a need for prehabilitation for cancer patients. The recently published *'Principles and guidance for prehabilitation within the management and support of people with cancer'* document provides case studies and information to clinicians of prehabilitation work for cancer patients throughout the country [79].

'Designing developing, and funding personalised cancer prehabilitation and rehabilitation: A How to Guide' [80], provides a comprehensive guide to what is and how to plan for implementing a prehabilitation service into an organisation. Cost calculators and examples of service design could help organisations make the business case for implementing prehabilitation services into their organisation.

Conclusion

Optimising the health, wellbeing and outcomes of lung cancer patients can be accomplished by offering them pre, peri and post treatment rehabilitation. Behavioural changes such as eating well, stopping smoking, and moving more, are established interventions with beneficial outcomes. Supporting lung cancer patients before, during and after their treatment may empower them to make positive lifestyle changes that will allow them to live well beyond their cancer treatments. Developing and implementing the right support package remains a challenge; to engage with and empower the patient in a timely fashion than meets with the national treatment timelines.

There is emerging evidence and examples of good practice which have been implemented into clinical pathways, signposting patients to support mechanisms. Sharing of exemplars and outcomes of research projects will continue the conversation to hopefully provide empirical evidence demonstrating the benefit to both patients and healthcare providers.

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