Review Article

The key questions in rehabilitation in thoracic surgery

Kajan Mahendran[1], Babu Naidu[1,2]

[1]Thoracic Surgery Department, Birmingham Heartlands Hospital, Birmingham, UK; [2]Birmingham Medical School, University of Birmingham, Birmingham, UK

Correspondence to: Babu Naidu. Thoracic Surgery Department, Birmingham Heartlands Hospital, Birmingham B9 5SS, UK. Email: b.naidu@bham.ac.uk.

Abstract: Enhancing the recovery of patients undergoing Thoracic Surgery is the raison d'être of a pulmonary rehabilitation (PR) process. Benefits of a PR program have been shown to include reduced postoperative complications, hospital length of stay (LOS) and improved exercise and lung function parameters. Identifying which groups of patients benefit most and the constituency of the perfect PR program is subject to ongoing research. Providing PR to patients in a manner acceptable to their lifestyle and disease timeline within economic limitations is the challenge.

Keywords: Pulmonary rehabilitation (PR); prehabilitation (PR); thoracic surgery

Submitted Mar 09, 2018. Accepted for publication Mar 22, 2018.
doi: 10.21037/jtd.2018.03.147
View this article at: http://dx.doi.org/10.21037/jtd.2018.03.147

What is it?

Rehabilitation from the Latin to 'again make fit' differs from prehabilitation (PR) which is defined as 'enhancing the functional capacity of an individual before an operation to enable him or her to withstand the stress of surgery (1). The outcome is a faster return to normal function, not just physical, but emotional and mental well-being too. Recovery after surgery can be impeded by the development of complications which aggravate the stress of surgery. Thus, measures to avoid these or reduce the impact of them are equally important. Conceptually PR is a functional process including optimising medical conditions, nutrition status and smoking cessation. An underpinning principle of enhanced recovery and fast track pathways, PR is diverse but, for this review, we will focus mainly on physical training which is usually considered to be a combination of aerobic exercises and strength training.

Why is it important?

Despite the advances in patient selection, surgery and perioperative care, short term complications and long-term sequelae from Thoracic surgery remain prevalent. Postoperative pulmonary complications (PPC) like pneumonia or respiratory failure lead to significantly longer length of hospital stay, intensive care admission and death (2). Patients who develop a PPC have worse overall and disease-free survival (3). Furthermore, patients undergoing major lung resection, when compared to age and gender matched controls, have significantly reduced mental and physical quality of life scores two years after surgery (4).

The importance of returning patients after surgery "back to normal" is brought into perspective by the massive task facing thoracic surgeons. On the topic of lung cancer alone worldwide there are 1.8 million new cases (5). Overall 5-year survival remains low between 8 and 17%, this despite modest improvements in care over the last few decades (6). Surgical resection remains the gold standard curative treatment, but resection rates remain low and widely variable (9–35%) between nations even within Europe (7). The peak incidence of age of diagnosis for lung cancer has risen from 60 in 1984 to 70–74 in 2008; an older population has a higher incidence of comorbid conditions (8). Thus, the challenge is to increase the proportion of patients we deem fit for surgery whilst reducing the postoperative morbidity.

Risk factors for complications include age, smoking status, poor lung function tests, malnutrition and co-morbidities (2,9). The prevalence of major comorbidities in thoracic surgery patients is especially high in lung cancer resection patients due to the strong association with age and smoking, chronic obstructive pulmonary disease (COPD)

(25–50%) and cardiovascular disease (25%). PR has an opportunity to impact all the above.

Exercise capacity is a key element in the selection process of patients suitable for thoracic surgery. Survival is also linked to exercise capacity at diagnosis of non-small cell lung cancer (10) and measures of response to exercise predict survival in lung disease (11,12). Complication rate, survival and success of surgery are linked to preoperative exercise capacity in various fields of thoracic surgery, including lung cancer (13-15) and lung volume reduction (16). Therefore, improving exercise capacity prior to surgery may be a means to improving outcomes afterwards.

Does it work?

Current clinical practice guidelines recommend that PR is considered for high risk patients undergoing a variety of thoracic surgical operations (17-19). PR is an important component of care in the management of patients with lung disease and has been shown to reduce the risk and impact of complications and enhance recovery after acute exacerbations (20).

Several recent systematic reviews and a meta-analysis have concluded that PR is beneficial but, because of heterogeneity of studies, the exact duration, intensity, structure and patient selection to achieve maximum efficacy is uncertain (21-23). Table (online: http://jtd.amegroups.com/public/system/jtd/jtd.2018.03.147-1.pdf) (24-42). summarises the key findings, in brief, studies reported a statistically significant improvement in peak oxygen consumption (VO2max) or in functional capacity measured with the 6-minute walk test from baseline to post-intervention. Lung function too is significantly enhanced after PR compared with baseline. Pooled estimates of effect sizes show a significant increase for both forced expiratory volume in 1 second (FEV1) [standardized mean difference (SMD) =0.27, 95% CI: 0.11–0.42] and FVC (SMD =0.38, 95% CI: 0.14–0.63).

Postoperative outcomes, specifically hospital length of stay (LOS) and morbidity, are significantly reduced in comparison with standard care. Pooled estimates of effect sizes show a significant reduction in both hospital LOS (mean difference = −4.83, 95% CI: −5.90 to −3.76) and PPCs (relative risk =0.55; 95% CI: 0.34–0.89; I^2 =27%) (23). The effect on PPC seems to be particularly to patients with poor lung function. Assessment of PR on Health-related quality of Life are limited by small numbers of studies and by the diversity and validity of tools used to assess. Currently there is no evidence to support that the addition of respiratory exercises to an exercise intervention provides any additional benefit in patients with COPD.

A further indicator of PR's benefit is presumed from measurements of exercise capacity. VO2max evaluation using cardiopulmonary exercise testing (CPET) represents the best independent predictor of surgical complication rate (43). When exercise capacity was poor (metabolic equivalents of <4) LOS nearly doubled in patients undergoing lung resection for cancer (44). Preoperative exercise programs improve VO2max. Increasing physical performance may result in better quality of life and reduce perceived dyspnoea in lung cancer resection patients (26,31).

The suggestion that exercise programs in patients with moderate to severe COPD are associated with less air leak thus significantly reducing chest tube days is an interesting idea. However, this was a finding of a small study, so findings will have been corroborated further (27).

PR can increase resection rates of lung cancer by improving measured characteristics of patients initially not considered fit for surgery based on pulmonary function and exercise test parameters (32,33). Morbidity was 15% and 25% respectively with no mortality in either of the small cohorts in these prospective studies.

Whilst the evidence for PR prior to thoracic surgery is generally supportive it has so far been cumulatively of low quality. Significant improvements in exercise capacity, lung function, complication rates and hospital LOS are seen. This data concurs with the emerging evidence in other areas of surgery that PR is beneficial (45,46).

What does the ideal PR program involve?

The ideology of a good program should be to physically and emotionally prepare the patient for surgery to enhance short and long term postoperative outcomes. Most of discussion thus far has centred around the exercise parameters of PR. Whilst supervised exercise programs form the cornerstone of PR, a comprehensive multidisciplinary approach which includes smoking cessation, nutrition, chronic disease optimisation, ensuring informed consent as well as ongoing patient selection are important components.

Complete smoking cessation is considered crucial by many surgeons. Risk of death and pulmonary complications is higher in smokers than those who have never smoked, and risk reduces with length of smoking cessation (47). LOS, ITU admission and risk of PPCs are significantly higher in smokers (48). Smokers who quit have a

higher abstinence rate when undergoing a supervised pulmonary rehabilitation (PR) program compared to usual treatment (49). However, access to smoking cessation programs can be poor. Providing smoking cessation care as part of the surgical pathway is preferred by patients (50).

Understanding and therefore engaging in the recovery process by the patient is an essential part of the consent process. Having multiple interactions with the multi-disciplinary extended surgical team can certainly enhance the process of information giving and processing (51).

Preoperative nutritional status is an important predictor of morbidity and mortality in renal, bladder and oesophageal cancer surgery (52-54). In COPD patients' nutritional parameters are often deranged, and protein metabolism is improved by supplementation with branched chain amino acids more so than aged matched controls (55). Many patients who undergo lung surgery have COPD. A prospective randomised study comparing a ten-day high nutrition diet to normal diet in patients undergoing lung cancer resection found significantly improved postoperative albumin levels with resultant lower complication rates and length of chest tube drainage time (56). A thorough nutritional assessment and intervention if required is a sensible adjunct to a PR programme.

What sort of exercise training?

In the five randomised controlled trials (RCT) and 15 other studies focusing on pre-rather than postoperative rehabilitation, the intervention was delivered mainly on an outpatient basis or in a training facility. The types of prescribed exercises included are summarised in *Table* (online: http://jtd.amegroups.com/public/system/jtd/jtd.2018.03.147-1.pdf) and generally involved aerobic training (lower and/or upper limbs) with addition in some studies of strength training. Respiratory exercises were included in most of studies. The addition of other elements such relaxation techniques, educational sessions *etc*. were inconsistent. The median duration was 4 (range, 1–10) weeks with a frequency of five sessions per week (range, 2–14) of moderate to high intensity generally tailored according to the patient's tolerance (21-23).

When should PR start and for how long?

A balance must be achieved between deriving the most benefit from a PR programme whilst not delaying surgery for cancer which could potentially progress. The rehabilitation programme should be instituted as early as possible even before a definitive decision for surgery has been made to maximize time on PR pathway.

The Swedish Lung cancer study group prescribed the ideal length of a rehabilitation programme to be 4–6 weeks (57). Treatment delays of up to 48 days have been shown not to impact survival - independently of cancer stage (58). However, Benzo *et al.* found that a four-week exercise program was not feasible due to patients and surgeons not willing to delay lung cancer surgery and therefore changed to more intense 1-week program (27). In the initial intervention group of 5 patients no improvement was seen in postoperative parameters and thus the study was stopped prematurely due to poor recruitment.

However other investigators have shown benefit in exercise regimes as short as 1 week (59) in terms of reduction in postoperative complications, hospital LOS and exercise parameters but without any demonstrable improvement in pulmonary function, emotional or dyspnoea scores (26,59).

Understanding that each patients' needs are different means that a PR programme may need to be tailored to the individual. For example, in one study 27 patients, initially considered unfit for surgery based on predicted postoperative FEV1, TLCO and VO2max, underwent a planned 4-week PR program. A third (9) of these patients required an extra two weeks before parameters met inclusion criteria for surgery (33).

Postoperative rehabilitation may also be important in improving patients' recovery. Lung resection patients who had rehabilitation starting 5–7 weeks after surgery for 20 weeks demonstrated improved exercise tolerance, functional fitness, muscle mass and strength compared to patients given standard postoperative hospital advice only on discharge (60).

Timing of rehabilitation is crucial, but it must be tailored to the individual patient and their disease process. When urgency of disease treatment is high, more intensive short regimes may be necessary to obtain the balance between surgical risk and benefit. Whilst the focus on reducing perioperative risk is high, postoperative rehabilitation must remain high on the agenda to help patients recover long term.

Which patients benefit from rehabilitation programs?

Several groups of patients may derive more benefit from rehabilitation programs.

A subgroup analysis of patients without impaired pulmonary function from a systematic review of patients undergoing lung cancer surgery showed the risk reduction for developing postoperative pulmonary complications was not significant. This reduced heterogeneity of results when this subset was removed from analysis (23).

From the general COPD cohort, patients demonstrate improved exercise capacity, arterial oxygenation, anxiety/depression scores after completing a course of rehabilitation. Patients with a higher exacerbation risk score benefitted from reduced frequency of exacerbations and hospital admissions (61). In operative lung cancer patients even mild COPD is associated with significantly higher risk of postoperative complications than those with normal lung function (62).

Patients with non-COPD related lung disease including Asthma, interstitial lung disease and cystic fibrosis/bronchiectasis also benefit from PR including measures of exercise capacity and quality of life (63). However, there is no evidence that rehabilitation is beneficial in patients with these conditions undergoing thoracic surgery.

Patients with advanced age and frailty index can safely undergo rehabilitation programs and show measurable benefit (64). In patients over 70 with no significant co-morbidities exercise training can reduce postoperative complications and reduce hospital LOS (59).

Even 'fit young' patients undergoing thoracic surgery can benefit from rehabilitation. For example, patients undergoing the NUSS procedure for pectus excavatum were found to have significantly improved exercise parameters if they underwent early postoperative rehabilitation. However, there was no significant difference in pain or lung function tests from control patients who did not have PR (65).

Where should rehabilitation happen?

Most PR programs studied are based in hospitals or specialist facilities. Home based rehabilitation programmes are both safe and efficacious (66). Indeed, in a comparison of in-hospital versus home based postoperative rehabilitation after cardiac surgery, equivalent improvements are observed in both groups (67). There is currently an ongoing trial comparing usual preoperative physical therapy to home-based rehabilitation in patients with non-small cell lung cancer awaiting resection (68). An app-based home exercise program may be an effective way to optimise uptake and deal with limitation to access to conventional outpatient-based rehabilitation whilst still preserving efficacy (69).

Conclusions

A pre and postoperative rehabilitation program can improve outcomes in patients undergoing thoracic surgery. Whilst this benefit has been shown in patients undergoing lung cancer surgery and lung volume reduction surgery, evidence is not robust. Heterogeneity among the studies in terms of participants and intervention make it difficult to draw definitive exact recommendations.

All patients can glean some benefit from tenets of a rehabilitation program, but it has not been delineated whether those at highest risk require longer periods of rehabilitation or whether the alternative of a more intense shorter program is equivalent. This is controversial where pathological stage, cultural and economic pressures impact on the timing to surgery. We cannot recommend delaying surgery to undergo PR in patients fit for surgery but in most health environments a period of 2 to 4 weeks is usually available between presentation to surgery to deliver this intervention.

With the advent of social media and app-based patient interaction across the population we are in a position to expand rehabilitation beyond current limitations of funding and facilities into the patients' home and to a wider variety of patient populations, pathologies and operations.

Acknowledgements

None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

References

1. Carli F. Prehabilitation to Enhance Postoperative Functional Capacity Following Radical Cystectomy. Trial description. Available online: http://clinicaltrials.gov
2. Agostini P, Cieslik H, Rathinam S, et al. Postoperative pulmonary complications following thoracic surgery: are there any modifiable risk factors? Thorax 2010;65:815-8.
3. Wang S, Li X, Li Y, et al. The long-term impact of postoperative pulmonary complications after video-assisted thoracic surgery lobectomy for lung cancer. J Thorac Dis 2017;9: 5143-52.
4. Möller A, Sartipy U. Long-term health-related quality of

life following surgery for lung cancer. Eur J Cardiothorac Surg 2012;41:362-7.
5. Ferlay J, Soerjomataram I, Ervik M, et al. GLOBOCAN 2012 cancer incidence and mortality worldwide: IARC cancerbase No. 11. Lyon, France: International Agency for Research on Cancer, 2013.
6. Coleman MP, Forman D, Bryant H, et al. Cancer survival in Australia, Canada, Denmark, Norway, Sweden, and the UK, 1995-2007 (the International Cancer Benchmarking Partnership): an analysis of population-based cancer registry data. Lancet 2011;377:127-38.
7. Wilking N, Hogberg D, Jonsson B. European benchmarking of lung cancer care. Journal of Clinical Oncology 2008;26:17535.
8. Castillo M. An overview of perioperative considerations in elderly patients for thoracic surgery: demographics, risk/benefit, and resource planning. Curr Opin Anaesthesiol 2018;31:1-5.
9. Lugg ST, Agostini PJ, Tikka T, et al. Long-term impact of developing a postoperative pulmonary complication after lung surgery. Thorax 2016;71:171-6.
10. Jones LW, Hornsby WE, Goetzinger A, et al. Prognostic significance of functional capacity and exercise behavior in patients with metastatic non-small cell lung cancer. Lung Cancer 2012;76:248-52.
11. Holland AE, Hill CJ, Glaspole I, et al. Impaired chronotropic response to 6-min walk test and reduced survival in interstitial lung disease. Respir Med 2013;107:1066-72.
12. Tojo N, Ichioka M, Chida M, et al. Pulmonary exercise testing predicts prognosis in patients with chronic obstructive pulmonary disease. Intern Med 2005;44:20-5.
13. Bolliger CT, Jordan P, Solèr M, et al. Pulmonary function and exercise capacity after lung resection. Eur Respir J 1996;9:415-21.
14. Benzo R, Kelley GA, Recchi L, et al. Complications of lung resection and exercise capacity: a meta-analysis. Respir Med 2007;101:1790-7.
15. Brutsche MH, Spiliopoulos A, Bolliger CT. Exercise capacity and extent of resection as predictors of surgical risk in lung cancer. Eur Respir J 2000;15:828-32.
16. Naunheim KS, Wood DE, Krasna MJ, et al. Predictors of operative mortality and cardiopulmonary morbidity in the national emphysema treatment trial. J Thorac Cardiovasc Surg 2006;131:43-53.
17. Nici L, Donner C, Wouters E, et al. American Thoracic Society/European Respiratory Society Statement on Pulmonary Rehabilitation. Am J Respir Crit Care Med 2006;173:1390-413.
18. Ries AL, Bauldoff GS, Carlin BW, et al. Pulmonary Rehabilitation: Joint ACCP/AACVPR Evidence-Based Clinical Practice Guidelines. Chest 2007;131:4S-42S.
19. Vogelmeier CF, Criner GJ, Martinez FJ, et al. Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Lung Disease 2017 Report: GOLD Executive Summary. American journal of respiratory and critical care medicine Am J Respir Crit Care Med 2017;195:557-82.
20. Spruit MA, Singh SJ, Garvey C, et al. An Official American Thoracic Society/European Respiratory Society Statement: Key Concepts and Advances in Pulmonary Rehabilitation. Am J Respir Crit Care Med 2013;188:e13-64.
21. Crandall K, Maguire R, Campbell A, et al. Exercise intervention for patients surgically treated for Non-Small Cell Lung Cancer (NSCLC): a systematic review. Surg Oncol 2014;23:17-30.
22. Mainini C, Rebelo PF, Bardelli R, et al. Perioperative physical exercise interventions for patients undergoing lung cancer surgery: What is the evidence? SAGE Open Med 2016;19:4:2050312116673855.
23. Sebio Garcia R, Yáñez Brage MI, Giménez Moolhuyzen E, et al. Functional and postoperative outcomes after preoperative exercise training in patients with lung cancer: a systematic review and meta-analysis. Interact Cardiovasc Thorac Surg 2016;23:486-97.
24. Pehlivan E, Turna A, Gurses A, et al. The effects of preoperative short-term intense physical therapy in lung cancer patients: a randomized controlled trial. Ann Thorac Cardiovasc Surg 2011;17:461-8.
25. Morano MT, Mesquita R, Da Silva GP, et al. Comparison of the effects of pulmonary rehabilitation with chest physical therapy on the levels of fibrinogen and albumin in patients with lung cancer awaiting lung resection: a randomized clinical trial. BMC Pulm Med 2014;14:121.
26. Stefanelli F, Meoli I, Cobuccio R, et al. High-intensity training and cardiopulmonary exercise testing in patients with chronic obstructive pulmonary disease and non-small-cell lung cancer undergoing lobectomy. Eur J Cardiothorac Surg 2013;44:e260-5.
27. Benzo R, Wigle D, Novotny P, et al. Preoperative pulmonary rehabilitation before lung cancer resection: results from 2 randomized studies. Lung Cancer 2011;74:441-5.
28. Li XH, Zhu JL, Hong C, et al. Effects of systematic re-habilitation programs on quality of life in

patients undergoing lung resection. Mol Clin Oncol 2013;1:200-8.
29. Fang Y, Zhao Q, Huang D. The impact of exercise training on surgery tolerability in lung cancer patients with impaired pulmonary function. Chin J Rehabil Med 2013;28:619-23.
30. Gao K, Yu PM, Su JH, et al. Cardiopulmonary exercise testing screening and pre-operative pulmonary rehabilitation reduce postoperative complications and improve fast-track recovery after lung cancer surgery: a study for 342 cases. Thorac Cancer 2015;6:443-9.
31. Bobbio A, Chetta A, Ampollini L, et al. Preoperative pulmonary rehabilitation in patients undergoing lung resection for non-small cell lung cancer. Eur J Cardiothorac Surg 2008;33:95-8.
32. Cesario A, Ferri L, Galetta D, et al. Pre-operative pulmonary rehabilitation and surgery for lung cancer. Lung Cancer 2007;57:118-9.
33. Divisi D, Di Francesco C, Di Leonardo G, et al. Preoperative pulmonary rehabilitation in patients with lung cancer and chronic obstructive pulmonary disease. Eur J Cardiothorac Surg 2013;43:293-6.
34. Jones LW, Peddle CJ, Eves ND, et al. Effects of presurgical exercise training on cardiorespiratory fitness among patients undergoing thoracic surgery for malignant lung lesions. Cancer 2007;110:590-8.
35. Mujovic N, Mujovic N, Subotic D, et al. Preoperative pulmonary rehabilitation in patients with non-small cell lung cancer and chronic obstructive pulmonary disease. Arch Med Sci 2014;10:68-75.
36. Bagan P, Oltean V, Ben Abdesselam A, et al. Pulmonary rehabilitation and prophylactic non-invasive ventilation before lung cancer surgery in very high-risk patients. Rev Mal Respir 2013;30:414-9.
37. Bradley A, Marshall A, Stonehewer L, et al. Pulmonary rehabilitation programme for patients undergoing curative lung cancer surgery. Eur J Cardiothorac Surg 2013;44:e266-71.
38. Peddle CJ, Jones LW, Eves ND, et al. Effects of presurgical exercise training on quality of life in patients undergoing lung re-section for suspected malignancy. Cancer Nurs 2009;32:158-65.
39. Coats V, Maltais F, Simard S, et al. Feasibility and effectiveness of a home-based exercise training program before lung resection surgery. Can Respir J 2013;20:e10-6.
40. Tarumi S, Yokomise H, Gotoh M, et al. Pulmonary rehabilitation during induction chemoradiotherapy for lung cancer improves pulmonary function. J Thorac Cardiovasc Surg 2015;149:569-73.
41. Sekine Y, Chiyo M, Iwata T, et al. Perioperative rehabilitation and physiotherapy for lung cancer patients with chronic obstructive pulmonary disease. Jpn J Thorac Cardiovasc Surg 2005;53:237-43.
42. Harada H, Yamashita Y, Misumi K, et al. Multidisciplinary team-based approach for comprehensive preoperative pulmonary rehabilitation including intensive nutritional support for lung cancer patients. PLoS One 2013;8:e59566.
43. Jones LW, Eves ND, Haykowsky M, et al. Cardiorespiratory exercise testing in clinical oncology research: systematic review and practice recommendations. Lancet Oncol 2008;9: 757-65.
44. Weinstein H, Bates A, Spaltro B, et al. Influence of Preoperative Exercise Capacity on Length of Stay After Thoracic Cancer Surgery. Ann Thorac Surg 2007;84:197-202.
45. Pouwels S, Stokmans RA, Willigendael EM, et al. Preoperative exercise therapy for elective major abdominal surgery: a systematic review. Int J Surg 2014;12:134-40.
46. Pouwels S, Hageman D, Gommans LN, et al. Preoperative exercise therapy in surgical care: a scoping review. J Clin Anesth 2016;33:476-90.
47. Mason DP, Subramanian S, Nowicki ER, et al. Impact of smoking cessation before resection of lung cancer: a Society of Thoracic Surgeons General Thoracic Surgery Database study. Ann Thorac Surg 2009;88:362-70; discussion 370-1.
48. Lugg ST, Tikka T, Agostini PJ, et al. Smoking and timing of cessation on postoperative pulmonary complications after curative-intent lung cancer surgery. J Cardiothorac Surg 2017;12:52.
49. Postolache P, Nemes RM, Petrescu O, et al. Smoking cessation, pulmonary rehabilitation and quality of life at smokers with COPD. Rev Med Chir Soc Med Nat Iasi 2015;119:77-80.
50. Farley A, Aveyard P, Kerr A, et al. Surgical lung cancer patients' views about smoking and support to quit after diagnosis: a qualitative study. J Cancer Surviv 2016;10:312-9.
51. Wen J, Schulman KA. Can Team-Based Care Improve Patient Satisfaction? A Systematic Review of Randomized Controlled Trials. PLoS One 2014;9:e100603.
52. Morgan TM, Tang D, Stratton KL, et al. Preoperative nutritional status is an important predictor of survival in patients undergoing surgery for renal cell carcinoma. Eur Urol 2011;59:923-8.

53. Gregg JR, Cookson MS, Phillips S, et al. Effect of preoperative nutritional deficiency on mortality after radical cystectomy for bladder cancer. J Urol 2011;185:90-6.
54. Zemanova M, Novak F, Vitek P, et al. Outcomes of patients with oesophageal cancer treated with preoperative chemoradiotherapy, followed by tumor resection: influence of nutritional factors. J BUON 2012;17:310-6.
55. Engelen MP, Rutten EP, De Castro CL, et al. Supplementation of soy protein with branched-chain amino acids alters protein metabolism in healthy elderly and even more in patients with chronic obstructive pulmonary disease. Am J Clin Nutr 2007;85:431-9.
56. Kaya SO, Seren S, Akcam TI, et al. Is preoperative protein-rich nutrition effective on postoperative outcome in non-small cell lung cancer surgery? A prospective randomized study. J Cardiothorac Surg 2016;11:14.
57. Myrdal G, Lambe M, Hillerdal G, et al. Effects of delays on prognosis in patients with non-small cell lung cancer. Thorax 2004;59:45-9.
58. BozcukH, Martin C. Does treatment delay affect survival in non-small cell lung cancer? A retrospective analysis from a single UK centre, Lung Cancer 2001;34:243-52.
59. Lai Y, Huang J, Yang M, et al. Seven-day intensive preoperative rehabilitation for elderly patients with lung cancer: a randomized controlled trial. J Surg Res 2017;209:30-6.
60. Edvardsen E, Skjønsberg OH, Holme I, et al. High-intensity training following lung cancer surgery: a randomised controlled trial. Thorax 2015;70:244-50.
61. Sahin H, Varol Y, Naz I, et al. The effect of pulmonary rehabilitation on COPD exacerbation frequency per year. Clin Respir J 2018;12:165-74.
62. Kim ES, Kim YT, Kang CH, et al. Prevalence of and risk factors for postoperative pulmonary complications after lung cancer surgery in patients with early-stage COPD. Int J Chron Obstruct Pulmon Dis 2016;11:1317-26.
63. Tonelli R, Cocconcelli E, Lanini B, et al. Effectiveness of pulmonary rehabilitation in patients with interstitial lung disease of different etiology: a multicenter prospective study. BMC Pulm Med 2017;17:130.
64. Salvi R, Meoli I, Cennamo A, et al. Preoperative high-intensity training in frail old patients undergoing pulmonary resection for NSCLC. Open Med (Wars) 2016;11:443-8.
65. Linhares SG, Pereira JC, Fernades PM, et al. Functional exercise capacity and lung function in patients undergoing an early rehabilitation program after the NUSS procedure: a randomized controlled trial. Pediatr Surg Int 2017;33:69-74.
66. Maltais F, Bourbeau J, Shapiro S, et al. Effects of home-based pulmonary rehabilitation in patients with chronic obstructive pulmonary disease: a randomized trial. Ann Intern Med 2008;149:869-78.
67. Scalvini S, Zanelli E, Comini L, et al. Home-Based Versus In-Hospital Cardiac Rehabilitation After Cardiac Surgery: A Nonrandomized Controlled Study. Phys Ther 2013;93:1073-83.
68. Laurent H, Galvaing G, Thivat E, et al. Effect of an intensive 3-week preoperative home rehabilitation programme in patients with chronic obstructive pulmonary disease eligible for lung cancer surgery: a multicentre randomised controlled trial. BMJ Open 2017;7:e017307.
69. Naidu B. Feasibility of the Fit4Surgery App - Can It Replace Conventional Pulmonary Rehabilitation in the Surgical Population? WCLC 2017 Poster Presentation.

Cite this article as: Mahendran K, Naidu B. The key questions in rehabilitation in thoracic surgery. J Thorac Dis 2018;10(Suppl 8):S924-S930. doi: 10.21037/jtd.2018.03.147

