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# THE CONCEPT OF PREHABILITATION IN THORACIC SURGERY: A SYSTEMATIC LITERATURE REVIEW

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## КОНЦЕПЦІЯ ПРЕАБІЛІТАЦІЇ В ТОРАКАЛЬНІЙ ХІРУРГІЇ: СИСТЕМАТИЧНИЙ ОГЛЯД ЛІТЕРАТУРИ

**І. Максим**

**Вступ.** Рак легенів є найпоширенішим видом раку в світі, він відповідає за 13,0% випадків усіх видів раку. Хірургічне втручання є оптимальним лікуванням операбельного раку легенів і підвищує виживаність цих пацієнтів. Однак, як і при будь-якій онкологічній операції, ускладнення є суттєвою причиною захворюваності та смертності. Програма попередньої реабілітації була запропонована як доопераційна допоміжна терапія для обходу даних наслідків, але існуючі дослідження показують суперечливі результати.

**Мета і завдання.** У цій статті ми розглядаємо еволюцію доказової бази для попередньої реабілітації перед резекцією легені, потенційні компоненти такої програми, а також як ці програми можна інтегрувати в план хірургічного лікування раку легенів і прагнемо визначити роль цієї програми. у підвищенні параметрів дихання та зменшенні післяопераційних ускладнень у пацієнтів.

**Матеріал і методи**. Було запитано пошук в електронних базах даних: PubMed, Clinicaltrials.gov, rcpjournals.org для рандомізованих клінічних досліджень, які досліджували ефективність концепції преабілітації та її вплив на функціональні параметри, післяопераційні ускладнення та якість життя пацієнтів. Первинною кінцевою точкою була здатність попередньої реабілітації підвищувати значення параметрів дихання у пацієнтів, які перенесли резекції легенів. Дослідженими вторинними параметрами були: післяопераційні ускладнення, оцінка функціональної здатності до і після операції, тривалість госпіталізації та вартість госпіталізації.

**Результати.** До огляду було включено десять клінічних досліджень (698 пацієнтів). Якість досліджень оцінювали за критеріями Delphi. Вплив цільової програми на покращення параметрів дихання пацієнтів

проаналізовано в 10 із 10 досліджень, частота респіраторних ускладнень у 9 із 10 досліджень та тривалість госпіталізації у 5 із 10 досліджень. Отримані результати можна віднести до категорії суперечливих, залежно від типу дослідження, розміру лотів та тривалості, інтенсивності та багатопрофільності програми реабілітації.

**Висновок**. Очевидно, що преабілітація має бути комплексно інтегрована в медичну практику, тому що це зрозуміла надія для онкохворих. Однак залишається очевидна потреба в оцінці ефективності програми попередньої реабілітації в конкретних групах населення.

**Ключові слова**: преабілітація, передопераційні вправи, параметри дихання, VATS, спірометрія, рак легенів.

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## THE CONCEPT OF PREHABILITATION IN THORACIC SURGERY: A SYSTEMATIC LITERATURE REVIEW

**I. Maxim**

**Introduction.** Lung cancer is the most common type of cancer in the world, responsible for 13.0% of cases of all cancers. Surgery is the optimal treatment for operable lung cancer and increases the survival rate of these patients. However, as with any oncological surgery, complications are a substantial cause of morbidity and mortality. The prehabilitation program has been proposed as preoperative adjuvant therapy to circumvent the given consequences, but existing studies show controversial results.

**Purpose and task**. In this article, we review the evolution of the evidence base for prehabilitation before lung resection, the potential components of such a program, and how these programs can be integrated into the surgical treatment plan for lung cancer and aim to identify the role of this program in elevating respiratory parameters and reducing patients' postoperative complications.

**Material and methods**. A search of the electronic databases was requested: PubMed, clinicaltrials.gov, rcpjournals.org for randomized clinical trials that investigated the effectiveness of the prehabilitation concept and its influence on functional parameters, postoperative complications, and patient's quality of life. The primary endpoint was the ability of prehabilitation to increase the values of respiratory parameters of patients undergoing lung resections. The secondary parameters investigated were: postoperative complications, functional capacity assessed pre- and postoperatively, length of hospitalization, and cost of hospitalization.

**Results.** Ten clinical trials (698 patients) were included in the review. The quality of the studies was assessed using Delphi criteria. The impact of the targeted program in improving the respiratory parameters of patients was analyzed in 10 out of 10 studies, the incidence of respiratory complications in 9 out of 10 studies and the duration of hospitalization in 5 out of 10 studies. The results obtained can be classified as controversial, depending on the type of study, the size of the lots and the duration, intensity and multidisciplinarity of the prehabilitation program.

**Conclusion.** It is obvious that prehabilitation needs to be comprehensively integrated into medical practice because this is a lucid hope for cancer patients. However, there remains a clear need to assess the effectiveness of the prehabilitation program in specific populations.

**Key words:** prehabilitation, preoperative exercises, respiratory parameters, VATS, spirometry, lung cancer.

**Introduction.** Lung cancer is the most common type of cancer worldwide, responsible for 13.0% of cases of all cancers [1]. The survival rate of lung cancer patients has improved at a fairly modest rate in recent decades [2]. In any case, for patients suffering from NMCLC in stage IA – IIA managed by surgery and adjuvant chemotherapy, the 5-year survival extends to 50% [2]. In recent years, the role of CT scanning with a minimum dose of radiation in the detection of lung cancer in the early stages has become increasingly essential [3, 4]. Given that these programs are implemented in parallel with the study of lung cancer, it is estimated that the number of patients identified at the early stage of NMCLC will increase.

Surgery is the optimal treatment for operable lung cancer and increases the survival rate of these patients. However, as with any oncological surgery, complications are a consistent cause of morbidity. Postoperative complications (POC) are associated with reduced survival, longer hospital stays, and a longer rate of intensive care monitoring. Like the impact on patient-centered outcomes, the impact on healthcare costs becomes considerable [5, 6].

In recent years, the role of perioperative interventions in reducing the risk of these complications has become more transparent to clinicians. The advancement and development of surgical recovery programs and postoperative pulmonary rehabilitation, together with preoperative rehabilitation strategies (prehabilitation) may have the potential to improve patient outcomes, as well as the possibility of ensuring operative convenience (elevating respiratory parameters for surgery). Most patients with lung cancer candidates for lung resection have as an associated pathology chronic obstructive pulmonary disease (COPD) and this means that a proportion is not suitable for surgery.

Prehabilitation did not appear as a topic in surgical textbooks in the 1980s. At that time, preoperative preparation for patients referred strictly to the correction of volume, intravascular fluids, and hydro-electrolyte balance. There were no large databases. Personal computers were underestimated at the time and became accessible only in the 1990s. Reports of surgical outcomes were usually based on laborious analysis of graphics from single institutions and were prone to subtle selection biases of the lead surgeon. In elective cases, patient selection was binary: either a patient was a surgical candidate or not.

The Goldman Criteria were published in 1977 [7]. This was a prospective benchmark study of preoperative variables that predicted cardiac events after major noncardiac surgery performed in 1001 patients over the age of 40 years. Data were collected from Massachusetts General Hospital from October 1975 to April 1976. Through multivariate discriminant analyzes, investigators were able to identify 9 predictors: the third heart sound or preoperative distension of the jugular veins, myocardial infarction in the previous 6 months; more than 5 premature ventricular contractions per minute before surgery; non-sinus rhythm or premature atrial contractions on the preoperative electrocardiogram; age over 70 years; intraperitoneal, intrathoracic or aortic surgery; emergency interventions; significant aortic or valvular stenosis; and compromised physical condition. Consequently, patients could be separated into 4 significantly different risk classes. Goldman criteria have become popular as a method of identifying the increased risk of elective surgery and a way to reduce the risk with synchronization and preoperative intervention.

Studies based on neoadjuvant chemoradiation for esophageal [8] and stage IIIA (N2) lung cancer [9, 10] in the mid-1990s have shown thoracic surgeons that dramatic but

temporary functional decline in somatic status could follow the neoadjuvant stage. The toxicity of combined chemoradiation frequently reduces the patient's performance. In the case of patients for whom the hope is to perform surgical resection after 4 weeks of neoadjuvant therapy, their somatic fragility interferes with the established plan. Upon further reassessment, clinicians found that the same physically vulnerable patients improved their strength and functional status through exercise, with a further 2 weeks to 6 weeks of recovery, thus making them strong enough for an operation. This experience has taught a generation of thoracic surgeons that the performance status of patients undergoing surgery could be improved before surgery.

Preoperative rehabilitation (prehabilitation) can optimize functional and nutritional capacity and can serve as a learning moment, in which lifestyle changes in a healthy one can be actively made [11]. Prehabilitation consists of two parts: (1) identifying preoperative conditions that are associated with postoperative morbidity and (2) attempting to minimize these preoperative conditions in the hope that they will provide better results. Moreover, when analyzing mortality after elective surgery, it is frequently characterized by multiorgan dysfunction.

Lung cancer surgery has a significant risk of postoperative lung complications. Through the integration of prehabilitation programs into lung cancer pathways, there are opportunities for long-term improvement in patient outcomes [12].

**Goals and objectives.** In this article, we review the evolution of the evidence base for prehabilitation before lung resection, the potential components of such a program, and how these programs can be integrated into the surgical treatment plan for lung cancer and aim to identify the role of this program in elevating respiratory parameters and reducing patients' postoperative complications.

**Material and methods.** The Review Protocol followed recommended methods by the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) [13].

*Data sources and search strategy*

We searched in electronically databases: PubMed, clinicaltrials.gov, rcpjournals.org for relevant studies in English for the last 6 years (February 2015 – September 2020) on thoracic surgery. Searching strategy included the following keywords: "prehabilitation", "preoperative exercises", "respiratory parameters", "spirometry", "lung cancer", "VATS".

*Inclusion criteria*

The inclusion criteria of the studies were: in extenso, 2015-2020, more than 25 patients.

*Exclusion criteria*

The exclusion criteria of the studies were: duplicate articles, without numerical parameters, less than 25 patients.

*Data extraction and assessment of the methodological quality of clinical studies*

The identified using the described search strategy references were reviewed: the abstract, the article content and it was filled in a table with the most relevant data. Data such as the number of patients, the type of surgery, the applied prehabilitation elements, the values of the parameters recorded were extracted and systematized in the table.

The assessment of the methodological quality of clinical studies was performed using the Delphi list, which identifies 9 criteria for assessing the quality of clinical trials [14].

**Results**

*Searching results*

The search results in the mentioned databases highlighted 346 potentially eligible citations, which were published between February 2015 and September 2020. After excluding the studies that were repeated (n = 49) or that did not match with the topic of the search by title or by abstract (n = 271), 26 articles remained that were studied in full text, in terms of inclusion criteria; only 10 studies met the established inclusion criteria [15–24] (figure 1).

*Assessment of methodological quality of studies*

The methodological quality of the studies was assessed according to the Delphi criteria [14]. Table 1 summarizes the evaluation of the methodological quality of the 10 selected clinical trials. All studies had specified patient eligibility criteria. Three studies [20, 22, 23] did not have similar patient groups according to most of the initial parameters. The evaluation of the variability of the primary outcome and the analysis of the intention to treat for postoperative outcomes was recorded in 10/10 studies.

*Characteristics of clinical trials*

The 10 included studies were summarized in Tables 2 and 3, and estimated the effectiveness of prehabilitation programs in patients with lung cancer, and recorded pre- and postoperative parameters. These were published between February 2015 and September 2020. A total of 698 patients were included in the studies. The size of the groups varied between n=26 and n =151, with an average of 27 patients. The studied surgical populations were as follows: open thoracotomies [15, 17, 18, 21], video-assisted thoracic surgeries [15, 16, 17, 18, 20, 22, 23, 24] and robot-assisted thoracic surgeries [23].

Mark L. (2016) [15] in a prospective study, on 151 patients, hypothesized that high-intensity interval training, could improve the functionality of the cardio-respiratory system prior to lung resections, in lung cancer. Patients suffering from operable lung cancer were randomly assigned to 2 groups: the control group (CG, N = 77) and the prehabilitation group (PG, N = 74). During the preoperative waiting period (approximately 25 days), VO2max and 6MWD increased (+ 15% [IQ 25–75%, + 9 to + 22%], respec-

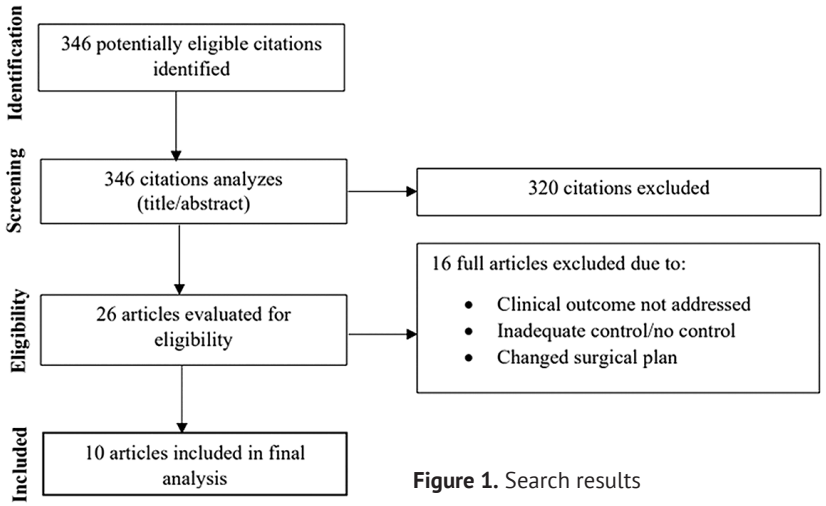


**Figure 1.** Search results

**Table 1**

*Assessment of methodological quality of studies, included for final analysis, by Delphi criteria*

| Clinical trial | Randomized? | Blind assigned program? | Similar groups from the start? | Specified eligibility criteria? | Blinded outcome assessors? | Patient blinded? | Blind medical staff? | Assessing the variability of the primary outcome? | Analysis of intention to treat for postoperative outcomes | Total quality score |
|---|---|---|---|---|---|---|---|---|---|---|
| Mark L. (2016) [15] | Yes | No | Yes | Yes | No | No | No | Yes | Yes | 5/9 |
| Zijia L. (2010) [16] | Yes | No | Yes | Yes | No | No | No | Yes | Yes | 5/9 |
| Laurent H. (2020) [17] | Yes | No | Yes | Yes | No | No | No | Yes | Yes | 5/9 |
| Gao et al. (2015) [18] | Yes | No | Yes | Yes | No | No | No | Yes | Yes | 5/9 |
| Francesco S. (2016) [19] | Yes | No | Yes | Yes | No | No | No | Yes | Yes | 5/9 |
| John B (2018) [20] | Yes | No | Not | Yes | No | No | No | Yes | Yes | 4/9 |
| Lai Y. (2017) [21] | Yes | No | Yes | Yes | No | No | No | Yes | Yes | 5/9 |
| Cavalheri V. (2017) [22] | Yes | No | No | Yes | No | No | No | Yes | Yes | 4/9 |
| Boujibar F. (2018) [23] | Yes | No | No | Yes | No | No | No | Yes | Yes | 4/9 |
| Garcia R. (2016) [24] | Yes | No | Yes | Yes | No | No | No | Yes | Yes | 5/9 |

*Note:* The list of Delphi criteria was established by the Delphi consensus for the assessment of methodological quality of clinical trials. A higher score indicates a better clinical trial quality.

tively, P = 0.003 and + 15% [IQ25-75, +8 to + 28%], P <0.001) in PG, VO2max decreased in CG (–8% [IQ25–75, –16 to 0%], P = 0.005).

The incidence of postoperative complications was not significantly different between the two groups: 27 of the 74 patients (35.5%) in PG and 39 of 77 patients (50.6%) in CG developed at least one of the postoperative complications (P = 0.080). It should be noted that the incidence of pulmonary complications was lower in PG compared to CG (23% vs 44%, P = 0.018), due to a significant reduction in atelectasis (12.2% vs 36.4%, P <0.001) and subsequently the duration of stay in intensive care (on average –7 hours, IQ25-75% –4 to –10).

Zijia L. (2020) [16], in his study of 73 patients, investigated the impact of a short-term, multimodal prehabilitation program conducted at home on the perioperative functional capacity of lung cancer patients, which follows to be subjected to lobectomy by VATS. The CG consisted of 36 patients and the PG of 37 patients who benefited preoperatively from a 2-week prehabilitation program. The mean 6MWD was 60.9 m higher perioperatively in PG compared to CG (95% [CI], 32.4-89.5; P <.001). Also, there were significant differences of the FVC parameter = 0.35 L, being higher in the prehabilitation group (95% CI, 0.05-0.66; P = .021).

Laurent H. (2020) [17] conducted a randomized study on 26 patients (CG = 14; PG = 12) in order to evaluate the effect of preoperative respiratory muscular endurance

**Table 2**

*Characteristics of the analyzed studies*

| Author Year Reference | Type of surgery | Applied prehabilitation elements | Recorded parameters |
|---|---|---|---|
| Marc Licker (2016) [15] n = 151 | PR (LE, PE) OT VATS | H – MIIT | *Preoperatively:* VO2 max; 6MWT; CPET *Postoperatively:* POC; duration of hospitalization; death rate |
| Aunt Liu (2020) [16] n = 73 | PR VATS | Aerobic Endurance exercises Breathing exercises Nutritional advice with protein supplements Psycho-emotional guidance Meditation | Preoperatively: 6MWT; 6MWD; Evaluation of lung function; Assessment of the degree of disability; Psychometric assessment *Postoperatively:* Quality of short-term recovery; Duration of hospitalization; POC; Mortality |
| Laurent H. (2020) [17] n = 26 | PR (LE; PE) VATS OT | Respiratory muscle endurance exercises | *Preoperatively:* Evaluation of lung function (EV, VO2 max), ET *Postoperatively:* POC (Clavien-Dindo classification); Duration of hospitalization; mortality |
| Gao et al. (2015) [18] n = 142 | PR (LE) VATS OT | Abdominal breathing exercises volumetr ic exerciser (Voldyne 5000, Sherwood Medical Supplies, St. Louis, MO, DOOR Volumetric Exercises (Sherwood Medical Supplies, St. Louis, MO) Exercises on the bike Drug therapy (antibiotics, bronchodilators, expectorants, corticosteroids) Smoking cessation | *Preoperator:* Evaluation of lung function; CPET *Postoperatively:* POC (pneumothorax, subcutaneous emphysema, diarrhea, allergic reactions, arrhythmias, lung infection,); Duration of hospitalization; The cost of rehabilitation |
| Francesco S. (2016) [19] n = 40 | PR (LE) | H – MIIT Breathing exercises Drug therapy (beta-2 agonists and / or anticholinergics, inhaled corticosteroids) | *Preoperatively:* Evaluation of lung function (FEV1, FVC, DLCO); degree of dyspnea (Borg scale); CPET *Postoperatively:* Postoperative complications; evaluation of lung function (FEV1, FVC, DLCO); degree of dyspnea (Borg scale); CPET |
| Giovanni B. (2018) [20] n = 32 | PR VATS | Yoga Breathing exercises (Pranayama technique) Smoking cessation | *Preoperatively:* Evaluation of lung function (FVC, FEV1, Tiffeneau-Pinelli index, PEF, PIF, SpO2, pulse). *Postoperatively:* POC; Evaluation of lung function (FVC, FEV1, Tiffeneau-Pinelli index, PEF, PIF, SpO2, pulse). |

**Continuation of the Table 2**

| Author Year Reference | Type of surgery | Applied prehabilitation elements | Recorded parameters |
|---|---|---|---|
| Lai Y. [21] (2017) n = 60 | PR OT | Abdominal breathing exercises Expiration exercises Aerobics through NuStep | *Preoperatively:* 6MWD; Life quality; Lung function; *Postoperatively:* Duration of hospitalization, POC. |
| Cavalheri V. [22] (2017) n = 96 | PR VATS | H – MIIT Exercises on the bike Endurance exercises | *Preoperatively:* 6MWD, VO2max, muscular endurance *Postoperatively:* Life quality; The degree of fatigue, depression; Lung function |
| Boujibar F. (2018) [2. 3] n = 38 | PR VATS RATS | Physical exercises Breathing exercises Smoking cessation | *Preoperatively:* Evaluation of lung function; CPET *Postoperatively:* POC; mortality |
| Garcia R. (2016) [24] n = 40 | PR VATS | H – MIIT | *Preoperatively:* 6MWT *Postoperatively:* POC, pulmonary POC (Melborne scale); Life quality; Duration of hospitalization, 6MWT |

PR – Pulmonary resection; LE – lobectomy; PE – pulmonectomy, VATS – Video assisted thoracoscopy; OT – Open thoracotomy, RATS – robotic-assisted thoracoscopy; CPET – cardiopulmonary exercise test, 6MWT – 6-minutes walking test; 6MWD – 6-minutes walking distance, H-MIIT – high intensity interval training, POC – postoperative complications; EV – Expiratory volume; ET – Endurance time, FEV1 – forced expiratory volume in one second; FVC – forced vital capacity; DLCO – carbon monoxide diffusion capacity; PEF – peak expiratory flow; PIF – peak inspiratory flow; SpO2 – oxygen saturation

training on respiratory functional parameters. The duration of the prehabilitation program was 3 weeks. Respiratory muscle strength increased significantly in PG compared to CG (+ 229 ± 199 compared to –5 ± 371 sec, P = 0.001). This increase was associated with a considerably lower number of postoperative pulmonary complications (2 vs. 10, P = 0.037).

Gao et al. (2015) [18] published another study, which included 142 patients in the risk group with potentially operable lung cancer. The patients were distributed in the study group (71 patients) who benefited from a preoperative lung prehabilitation program followed by lobectomy, the other half being distributed in the control group (71 patients) who underwent only lobectomy with conventional treatment. The intervention program consisted of 2 sessions per day, of 30-40 min during 3–7 days. The rate of total postoperative complications in PG (16.90%) was significantly lower than in CG (83.31%) (P = 0.00), as was the rate of postoperative pulmonary complications (CPP): PG (12.81%) versus CG (13.55%) (P = 0.009). There was no difference between groups in terms of the cost of hospitalization (P = 0.304).

Francesco S. (2016) [19] in his study based on 40 patients, proved that the prehabilitation program is a valid preoperative strategy, aimed at improving physical performance in patients with non-microcellular lung cancer, with associated COPD;

these performances are maintained even late postoperatively. Forty patients were analyzed with both NMCLC and COPD, aged <75 years, TNM stages I-II, who underwent lobectomy. Patients were randomly divided into two groups (PG and CG): PG followed an intensive preoperative program, while CG underwent only surgery (lobectomy). The VO2max parameter was evaluated in all patients at time 0 (T0), after prehabilitation / before surgery in PG versus CG (T1) and 60 days after surgery, respectively, in both groups (T2). To clarify the role of pulmonary prehabilitation, the effects of high-intensity preoperative training, lasting up to 3 weeks, on physical performance and respiratory function were evaluated. Significant differences between batches were detected directly at the VO2max parameter, in favor of the prehabilitation batch.

Giovanni B. (2018) [20] in his prospective study based on 32 patients studied the benefits of yoga breathing exercises on lung function. Parameters such as FVC, FEV1, Tiffeneau-Pinelli index, PEF, PIF, SpO2, heart rate were analyzed in 3 benchmarks: initial (T0), preoperative (T1) and postoperative (T2). The results demonstrate a significant short-term improvement in lung function, assessed by spirometry. Pranayama meditative short-circuit breathing exercises have proven to be amazingly effective in raising the values of functional parameters and increasing the quality of life of these patients.

Lai Y. (2017) [21] conducted a prospective randomized controlled study with a total of 60 subjects aged ≥ 70 years. The intervention group was treated for 1 week with systematic and very intense preoperative training before lobectomy, and the control group was supported with conventional preoperative respiratory management. The 6-minute walking distance (6-MWD), peak expiratory flow (PEF) and quality of life scores before and after the prehabilitation regimen, as well as the incidence of postoperative pulmonary complications were analyzed. Significant differences between groups were recorded in terms of postoperative complications and the duration of hospitalization of these patients.

Cavalheri V. (2017) [22] in his randomized study analyzed the influence of prehabilitation on several indices that would characterize the quality of life of patients with NMCLC after surgery. Ninety-six patients were analyzed and divided into 2 groups: PG which was n = 48 and CG, n = 48. Patients followed a complex program of H – MIIT exercises, cycling and resistance exercises. Parameters that were recorded preoperatively: 6MWD, VO2max, muscular endurance, postoperative: quality of life; the degree of fatigue, depression; lung function.

Boujibar et al. (2018) [23] reported their results in a study in order to determine whether participating in a prehabilitation program would improve outcomes after surgery and decrease morbidity according to the Clavien-Dindo classification. The cohort included 38 patients with potentially operable lung cancer and VO2 max ≤20 mL / min / kg. A higher number of patients with the Clavien-Dindo score ≤2 followed the prehabilitation program compared to those in CG, respectively 17/19 vs. 8/15; P = 0.0252. Consequently, a smaller number of patients in PG compared to those in CG, had postoperative complications, respectively 8/19 vs. 12/15; P = 0.0382.

Garcia R. (2016) [23] developed a randomized clinical trial based on 40 patients to be treated by total lung resection. The candidates were divided into 2 groups (PG and CG), the first following an intensive combined program that included physical exercises and resistance exercises. The author states that the prehabilitation program can improve cardiopulmonary functionality despite the fact that there were no significant differences between groups at all analyzed parameters. After training, there was a statisti-

cally significant improvement in exercise tolerance (+397 seconds, p = 0.0001), physical component (+4.4 points, p = 0.008) and muscle strength (p <0.01). Patients were evaluated at baseline (before randomization), preoperatively (PG only), postoperatively, and three months postoperatively.

In 4/10 studies, high-intensity interval training was applied [15, 19, 22, 24], in 6/10 breathing exercises [16, 18, 19, 20, 21, 23] and in 3 / 10 muscular endurance exercises [16, 17, 22]. The prehabilitation program was supplemented with drug therapy (antibiotics, bronchodilators, expectorants, corticosteroids, anticholinergics) in 3/10 studies [16, 18, 19]. Smoking cessation was applied in 3/10 studies [18, 20, 23], and nutritional counseling in 2/10 studies [16, 18]. Giovanni B.'s study [20] had a special approach to this program, implementing the Pranayama technique as the basic technique in prehabilitation of patients undergoing pulmonary lobectomy, finally recording astonishing results of respiratory parameters.

For a nonlinearity of the prehabilitation program, 7/10 studies opted [16, 18, 19, 20, 21, 22, 23], 3/10 studies were followers of monodisciplinary programs (H – MIIT) [15, 24]. The intensity of the applied prehabilitation techniques also varied, 5/10 studies subjected the patients to moderate – advanced physical effort [15, 16, 19, 22, 24].

All 10 studies recorded the parameters in 3 stages: before the start of the program, pre- and later postoperatively. In the study of Garcia R. [23] the results were recorded both preoperatively, immediately postoperatively and late postoperatively (3 months after intervention).

*The efficiency of the prehabilitation program*

The efficiency of the prehabilitation program in reducing the rate of postoperative complications and increasing the values of functional parameters was demonstrated in 10/10 studies, systematized in table 3.

The results obtained in the 10 studies were divided into two categories: no significant differences between groups and with significant differences between groups. Consequently, 4/10 studies recorded significant differences between batches of the *6MWD* parameter (6-minutes walking distance) [15, 16, 22, 24]. Garcia R.'s study [24] recorded bewildering results, exclusively of the given parameter, compared to the other parameters analyzed. The author states that in these patients, preoperative exercises could play an important role in preventing functional decline after surgery, while accelerating postoperative recovery. It should be noted that the study of Mark L. [15] who opted for a program that includes only H-MIIT (high-intensity-moderate-intensity physical training) compared to other studies [16, 18, 19, 20, 21, 22, 23] who approached multidisciplinary patients, obtained promising results of the 6MWD parameter (+15% in PG versus –8% in CG).

*CPET* (cardiopulmonary exercise test) parameters were processed in 4/10 studies [15, 18, 19, 23], of which in 3/10 no significant differences were found between groups [18, 19, 23]. Significant differences between batches of CPET parameters (+ 8% in PG) can be noticed in the prospective study of Mark L. [15].

Regarding *respiratory parameters*, such as VO2max, FVC, FEV1, VEM, VE, ET, PEF, PIF studies tend to push the limits, orchestrating the results obtained with conclusive values in this consensus. In 6/10 studies, significant differences were registered between groups in terms of respiratory functional explorations [15, 16, 17, 19, 20, 22]. Laurent H.'s study [17] was limited to a total number for both groups of 26 patients, and to reveal the effects of the prehabilitation program on functional parameters, larger groups

**Table 3**

*The results of the analyzed studies*

| Author Year Reference | Main outcomes | Conclusions |
|---|---|---|
| Marc Licker (2016) [15] n = 151 | *No significant differences between lots:* Postoperative complications (35.5% in PG, 50.6% in CG), P = 0.080, duration of hospitalization (9 versus 10 days), P = 0.080 *With significant differences between lots:* VO2 max (+ 15% in PG, –8% in PG), P = 0.003 6MWT (+ 15% in PG, –8% in PG), P <0.001 CPET (+ 8% in PG), P = 0.005 | Consequently, the harmlessness and effectiveness of the short-term intensive training program have been demonstrated. However, the targeted improvements failed to produce significant differences in morbidity-mortality rates compared to regular care. |
| Aunt Liu (2020) [16] n = 73 | *No significant differences between lots:* FEV1, postoperative complications, length of hospital stay *With significant differences between lots:* 6MWD (+ 60.9 m at PG compared to CG (95% confidence interval [CI], 32.4–89.5; P <0.001) FVC (L) (+0.35, 95% CI, 0.05–0.66; P = 0.021) VEM (L / min) (+19.8 (–21.0 vs 61.2) P = 0.339 | This study is the first randomized study that combines aerobic exercise with physical endurance, breathing exercises, nutrition, and psychological support in a multimodal prehabilitation program. Despite the limitations to which this study was subjected, the authors were able to demonstrate the effectiveness of the program in increasing the values of parameters such as 6MWD, FVC and VEM). |
| Laurent H. (2020) [17] n = 26 | *No significant differences between lots:* Duration of hospitalization, VO2 max. *With significant differences between lots:* Postoperative pulmonary complications (2 vs. 10, P = 0.037) EV and ET increased only in PG (+ 15 ± 16 vs. –2 ± 17 l / min –1 and + 229 ± 199 vs. –5 ± 371 sec, respectively; P = 0.004 and P = 0.001, respectively) | This study recorded positive results in EV and ET, following the heterogeneous prehabilitation program. These results should be confirmed in larger randomized controlled trials, including a larger number of patients, especially with pathological changes in respiratory muscle function. |
| Gao et al. (2015) [18] n = 142 | *No significant differences between lots:* CPET, FEV1, cost of hospitalization (no difference) *With significant differences between lots:* Postoperative complications (16.9% in PG and 83.3% in CG), P = 0.00 Duration of hospitalization (7.21 versus 11.07 days), P = 0.00 | There were no significant changes in preoperative parameters, these being useful only in detecting patients at high risk for postoperative complications. In conclusion, the effectiveness of the prehabilitation program was demonstrated, which decreased the complication rate in PG compared to CG. |
| Francesco S. (2016) [19] n = 40 | *No significant differences between lots:* FEV1, postoperative complications, CPET *With significant differences between lots:* Preoperative VO2max (17.8 ± 2.1 in PG and 14.5 ± 1.2 in CG (76.1 ± 14.9 vs 60.6 ±8.4), P<0.0001 (<0.05); Late postoperative VO2max (15.1 ± 2.4 in PG and 11.4 ± 1.2 in CG (64.6 ± 15.5 vs 47.4 ± 6.9), P <0.05 (<0.05). | Based on the data obtained in this study, it is possible to state that high-intensity prehabilitation improves the physical performance of patients with COPD and NMCLC undergoing surgery, compared to similar surgical patients who did not follow this program. These differences were not present at the initial assessment, but became apparent after the prehabilitation program and continued to emerge after the surgery. |

**Continuation of the Table 3**

| Author Year Reference | Main outcomes | Conclusions |
|---|---|---|
| Giovanni B. (2018) [20] n = 32 | *No significant differences between lots:* Heart rate *With significant differences between lots:* **FVC** (T0 (%) 83.1 ± 15.6 – 92.2 ± 16.8 FVC T1 (%) in PG and 95.0 ± 15.6 – 94.0 ± 17.2 in CG); FEV1 (T0 (%) 75.7 ± 10.6 – 93.1 ± 20.6 FEV1 T1 (%) in PG and 93.4 ± 16.2 – 90.9 ± 20.5 in CG); TIFF (56.2 ± 7.2 – 60.1 ± 6.7 in PG vs 61.8 ± 8.1 – 59.2 ± 7.9 in CG); **PEF** (56.1 ± 20.0 – 69.9 ± 19.2 in PG vs 70.3 ± 27.8 – 65.3 ± 31.2 in CG); **PIF** (35.3 ± 16.1 – 45.8 ± 17.5 in PG and 41.1 ± 22.9 – 43.4 ± 27.3); **SpO2**(94.8 ± 1.0 – 99.6 ± 1.0 in PG, 95.9 ± 0.6 – 96.8 ± 0.6 in CG). | This study contributes to the in-depth knowledge of the benefits of meditative pranayama practice on impaired lung function of active smokers. Although standard breathing exercises are effective to some extent, yoga breathing is an alternative option that can provide optimal short-term improvement of lung function. Thus, yoga breathing can become a valid support for preoperative training in thoracic surgery. Moreover, yoga breathing has the potential to help smokers quit smoking and improve their quality of life. |
| Lai Y. [21] (2017) n = 60 | *No significant differences between lots:* Pulmonary function (PEF), 6MWD *With significant differences between lots:* CPO (PG: 4 out of 30 (13%) CG: 11 out of 30 (37%) P = 0.037 Duration of hospitalization (PG: 6.9 ± 4.4 days, CG: 10.7 ± 6.4 days P = 0.01) | This study investigated the short-term prehabilitation program, combined with inspiratory muscle training and aerobic endurance training in elderly patients scheduled to undergo lobectomy. For elderly patients with NMCLC who are about to undergo surgery in China, an intensive 7-day prehabilitation model combined with aerobic endurance training may be a feasible preoperative strategy with positive physical and psychological effects. |
| Cavalheri V. [22] (2017) n = 96 | *No significant differences between lots:* Lung function (FEV1, FVC); Degree of fatigue, depression *With significant differences between lots:* 6MWD (95 ± 5 in PG and 76 ± 16% in CG, (p = 0.09) VO2max (70 ± 21 in PG and 62 ± 13% in CG, (p = 0.74) | This study outlines the fact that the prehabilitation program had a positive impact on the somatic capacity of patients, increasing their performance and the results of the 6MWD test and the VO2max parameter. It should be noted that adherence to the program was poor, which would probably have compromised the effectiveness of the program. |
| Boujibar F. (2018) [23] n = 38 | *No significant differences between lots:* CPET, FEV1, length of hospital stay (no difference) P = 0.644 *With significant differences between lots:* Postoperative complications (42% in PG, in CG 80%), P = 0.0382 (Clavien-Dindo gr. 2 and less), P = 0.0252 | The results of this study suggest that prehabilitation has a positive impact on the occurrence and severity of postoperative complications. Prehabilitation is easy to achieve and easy to adapt to the functional abilities of each patient. Prehabilitation should be considered systematically in patients with non-microcellular lung cancer to reduce perioperative risks and not to limit the lung function of these patients. |

**Continuation of the Table 3**

| Author Year Reference | Main outcomes | Conclusions |
|---|---|---|
| Garcia R. (2016) [24] n = 40 | *No significant differences between lots: CPO, pulmonary CPO (Melborne scale); Life quality; Duration of hospitalization, With significant differences between lots:* 6MWD (507.7 ± 9 in PG vs. 420.2 ± 116.3 in CG) | The results of the study suggest that a preoperative exercise-based program may improve somatic capacity, muscle strength and physical component of quality of life in patients with lung cancer. In these patients, preoperative exercise could play an important role in preventing functional decline after surgery while accelerating postoperative recovery. |

PG – Prehabilitation group; CG – Control group, EV – Expiratory volume; ET – Endurace time; NMCLC – Non-microcellular lung cancer

may be needed. Despite the limitations of any kind, to which were subjected the studies, the results are encouraging, initiating stridor of perspective, because 6/10 studies record positive results in this context.

Mark L.'s study [15] offers a strong increase of up to 15% of VO2 max in favor of the prehabilitation program, while the prospective study of Zijia L. [16] records values of up to 19.8% of the VEM parameter. The studies of Francesco S [19] and Cavalheri [22], despite the fact that adherence to their programs was poor, and could compromise its effectiveness, were able to show that the increase in respiratory parameters began to be evident both preoperatively and after the intervention. Particular attention should be paid to the study, at least uncommonly by Giovanni B. [20], which contributed to the subtlety and depth of knowledge of the benefits of Pranayama meditative practice on compromised lung function of smokers with NMCLC. The author marks good results of respiratory parameters (FVC, FEV1, TIFF, PEF, PIF, $SpO_2$) in these patients who have joined the lung prehabilitation program based on the Pranayama breathing technique.

If we refer to the criterion of *hospitalization duration*, out of 7 studies [15, 16, 17, 18, 21, 23, 24] that approached this criterion, only 1 of them [18] registered significant differences between groups at the given parameter. The analyzed studies also did not prove the influence of the prehabilitation program in reducing the cost of hospitalization of these patients (parameter interdependent with the duration of hospitalization of patients).

A certain degree of control over the prehabilitation program is maintained by the monitoring of *postoperative complications*, which, in addition to the other indicators, play a substantial role in clarifying the effectiveness of this program. This parameter was analyzed in 8/10 studies [15, 16, 17, 18, 19, 21, 23, 24], 4/10 studies registered significant differences between the two groups in this chapter [17, 18, 21, 2. 3]. In the study of Laurent H. [17] were detected only 2 cases out of 13, of postoperative pulmonary complications in PG, while in CG – 10/13 cases. Gao et al. [18] demonstrated the effectiveness of the prehabilitation program, which decreased the complication rate in PG (16.9%) compared to CG (83.3%). The results of the study by Boujibar F. [23] suggest

that prehabilitation has a positive impact on the occurrence and severity of postoperative complications (42% in PG, in CG 80%). The study by Lai Y. [21] who investigated the short-term prehabilitation program (7 days) demonstrates that it can be a feasible strategy to reduce postoperative complications and accelerate prehabilitation with positive physical and psychological effects (POC – PG: 4 of 30 (13%) CG: 11 of 30 (37%).

**Discussion.** As the promotion and development of postoperative prehabilitation arouse more and more interest, prehabilitation has become known as a safe and promising mean of elevating the vital functions of patients in their surgical training but also catalysing the recovery process after surgery.

Exercise, whether supplemented by other practices or not, is a substantial stimulus in increasing the somatic performance of candidates for surgery, thus preparing them both physically and psychologically for this event.

In the last decade, there has been a lucidity in realizing that a successful surgery does not depend only on the surgery itself, but rather on how well the patient is prepared to return to an adequate physical and psychological status [25, 26, 27]. The purpose of this review is to highlight the importance of a proactive preoperative multimodal approach and patient recovery after surgery.

Three months after a major elective surgery, up to 50% of patients still have a degree of disability [28]. As an objective of accelerated and improved recovery of protocols is to shorten the duration of hospitalization, it is important that patients can function well physically, and be relatively self-sufficient and physically independent on hospital discharge. A major determinant of recovery is surgical morbidity, as complications have a significant impact on the postoperative physical condition and overall quality of life of the patient.

In fact, despite limited data in the literature, the results of this review show that the prehabilitation program, along with pharmacological optimization and smoking cessation, is an important strategy for improving the outcome of the intervention. This approach seems more crucial because prehabilitation could increase the number of patients eligible for surgery.

Unfortunately, we could not find an answer to the question whether the application of the concept of prehabilitation would excuse the error of admission of patients or rather, the mistake made in the inclusion criteria.

What is certain is that we can deny the utopia of this concept, as an argument are the astounding results that were recorded in the previously analyzed studies. For example, the study by Giovanni B. [20], which contributes to the benefits of pranayama meditative practice on lung function in active smokers affected by lung cancer scheduled for surgery, shows amazing results of all respiratory parameters, which are in fact the gold standard in thoracic surgery. Although breathing exercises are effective to some extent, yoga breathing is an alternative option that can provide optimal short-term improvement in lung function. Thus, yoga breathing can become a valid support for preoperative training in thoracic surgery. Moreover, yoga breathing has a potential to help smokers quit this habit and improve their quality of life.

The dichotomy of this subject is further dispersed with the emergence of numerous studies that unconvincingly promote this concept. Lack of adherence on the one hand and transparency on the other, are the main reasons why the prehabilitation program is not included in the national protocols, and consequently is not implemented by clinicians.

**Conclusions.** Prehabilitation is a conventional wisdom of the time. Lost in depth and rediscovered today, this concept can revolutionize the clinical dimension of large surgery, becoming a hope of candidates for surgery.

It is clear that prehabilitation needs to be comprehensively integrated with other elements of an improved recovery program to maximize its effectiveness. However, there remains a clear need to assess the effectiveness of prehabilitation in specific populations using appropriate measures and valid values, as well as to determine whether multimodal interventions can reduce the risk of developing long-term disability in high-risk patients. Finally, the impact of prehabilitation on healthcare use, cancer treatment, response to surgery and postoperative stress and complications needs to be further elucidated.

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