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THE CONCEPT OF PREHABILITATION AND ITS IMPACT IN SURGERY: A SYSTEMATIC LITERATURE REVIEW

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ПОНЯТТЯ ПРЕАБІЛІТАЦІЇ ТА ЇЇ ВПЛИВ В ХІРУРГІЇ: СИСТЕМАТИЧНИЙ ОГЛЯД ЛІТЕРАТУРИ

І. Максим

Вступ. Значна кількість пацієнтів, які перенесли операцію, страждають від післяопераційних ускладнень. Ця проблема стала нагальною, її поширеність становить близько 30% серед пацієнтів, які проходять хірургічне лікування. Програма попередньої реабілітації була запропонована як доопераційна допоміжна терапія для того, щоб обійти дані наслідки, але існуючі дослідження показують суперечливі результати.

Мета і завдання. Систематичний огляд літератури спрямований на вивчення ефективності концепції пререабілітації та її впливу на функціональні показники, післяопераційні ускладнення та якість життя 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. Основним параметром результату була здатність попередньої реабілітації запобігти післяопераційним ускладненням у пацієнтів, які перенесли серйозні операції. Дослідженими вторинними параметрами були: оцінена функціональна здатність до і після операції, тривалість перебування в стаціонарі, вартість госпіталізації та якість життя після операції.

Результати. Огляд включав 10 клінічних досліджень загалом 939 пацієнтів. Якість досліджень оцінювали за критеріями Delphi. У 10 із 10 досліджень досліджувався вплив цільової програми на зменшення післяопераційних ускладнень пацієнтів, тривалість госпіталізації у 7 із 10 досліджень та параметри дихання у 4 із 10 досліджень.

Висновки. Потрібні широкомасштабні високоякісні дослідження, щоб підтвердити перспективи ранніх доказів і визначити частоту, інтенсивність та тривалість попередньої реабілітації, призначеної для досягнення оптимальних результатів.

Ключові слова: реабілітація, передопераційні вправи, післяопераційні ускладнення, великі операції, функціональні параметри, огляд літератури.

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THE CONCEPT OF PREHABILITATION AND ITS IMPACT IN SURGERY: A SYSTEMATIC LITERATURE REVIEW

I. Maxim

Introduction. An impressive number of patients who undergo surgery suffer from postoperative complications. This problem has become imperative, with a prevalence of about 30% among patients undergoing surgical treatment. The prehabilitation program has been proposed as preoperative adjuvant therapy in order to circumvent the given consequences, but existing studies show controversial results.

Purpose and task. The systematic literature review aims to study the effectiveness of the concept of prehabilitation and its influence on the functional parameters, the postoperative complications, and the quality of life of patients.

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 patients' quality of life. The primary outcome parameter was the ability of prehabilitation to prevent postoperative complications of patients undergoing major surgery. The secondary parameters investigated were: the functional capacity evaluated pre- and postoperatively, the length of hospital stay, the cost of hospitalization, and the quality of life after surgery.

Results. The review included 10 clinical trials with a total of 939 patients. The studies' quality was evaluated using Delphi criteria. In 10 of the 10 studies, the impact of the targeted program on reducing postoperative complications of patients was examined, as was the duration of hospitalization in 7 of the 10 studies, and respiratory parameters in 4 of the 10 studies.

Conclusions. Large-scale, high-quality studies are required to confirm the early evidence's promise and to determine the frequency, intensity, and duration of prehabilitation designed to accomplish optimal results.

Key words: prehabilitation, preoperative exercises, postoperative complications, major surgeries, functional parameters, literature review.

Relevance and problem statement. Prehabilitation is a practice used to improve postoperative outcomes by increasing the patient's functional capacity prior to surgery. The concept of prehabilitation is headed for a multifactorial approach, that includes medical optimization, preoperative exercise, nutritional support, and stress/anxiety reduction [1].

Despite continuous surgical advances (with a tendency towards minimal invasiveness) and anesthetics (subsequently postoperative analgesia), invasive cancer treatment remains a challenge that requires substantial physiological and mental resistance from the patients. But even in the absence of complications, an ample group of patients is not capable to regain their capacity and preoperative somatic status, after surgery.

Surgical interventions involving a complex body cavity cause a global neuroendocrine inflammatory response, imposing a significant physiological voltage [2]. Surgery induces a „stress response" which activates the hypothalamic–pituitary–adrenal axis and sympathetic nervous system, leading to proteolysis and lipolysis providing substrates for gluconeogenesis [3, 4].

An impressive number of patients who are subjected to surgery (regardless of its invasiveness) fight with postoperative consequences. Approximately 30% of patients following major surgery suffer postoperative complications, but even in their absence, they are associated with reducing the functional capacities of patients [5]. Vulnerable patients, such as the elderly and those with associated pathologies (COPD, DM, MI, STROKE history) are largely about post- and peri-operative morbidity and mortality.

For the first time, the concept of prehabilitation was addressed in the article "Prehabilitation, Rehabilitation, and Revocation in The Army" ("Prehabitation, Rehabilitation, and Revocation in the Army") published in the British Medical Journal, 1946 [6]. The article tells how many of the men presenting for enlistment during the Second World War were rejected because of their poor physical and mental conditioning – a by-product of poverty, malnutrition, and poor education – and how over 2 months, these substandard recruits were transformed by a program of educational, physical, and nutritional interventions into standard recruits. Of the 12 000 men who passed through prehabilitation centers, more than 85% improved both physically and mentally.

Subsequent articles have emerged in the dimension of the imperative need for the concept given in order to avoid undesirable consequences. Only in the 1980s, studies about prehabilitation gradually reappeared. These were outlined in the "Sports Medicine" community and focused on the idea of prehabilitation as a means of preventing lesions in athletes. With the emergence of the first systematized revisions, the importance of the concept has received refractivity in thoracic and abdominal surgery. One of the earliest systematic reviews was published in 2011 [7]. The review of 1245 patients recruited to 12 randomized controlled trials found that patients undergoing cardiac and abdominal surgery experienced shorter hospital stays and reduced postoperative pulmonary complication rates if they had received preoperative exercise therapy.

The ERAS (Enhanced Recovery After Surgery) guideline offers modest prehabilitation programs, focusing its efforts on the development of postoperative rehabilitation. However, rehabilitation does not improve muscle and functional reserves since patients are involved in magnitude surgery.

Exercise, the basis of existing prehabilitation programs, aims to improve a patient's functional capacity through structured regimens including combinations of aerobic, resistance and inspiratory muscle training. Research has shown that exercise programs are more successful if they offer a multimodal approach combining other facets including nutritional and psychological arms [8, 9].

Evidence for cardiac, pulmonary, and major abdominal surgery [10, 11], indicates that preoperative diaphragmatic and respiratory muscle training, including incentive spirometry and coughing exercises, can improve numerous postoperative outcomes.

However, the challenge lies in the fact that when it goes for major surgery (either for lung or abdominal cancers), there is an opportunity window, an average of 4–6 weeks, to undertake the desired prehabilitation measures for given patients. This window can provide added precision in the diagnosis and staging of tumor invasion, clinician/surgeon having time to ensure the accuracy of the preoperative diagnosis.

The ambivalence of the concept of prehabilitation is widely discussed in the scientific literature. On the one hand, it takes time to follow an efficient prehabilitation program that would include many (physical, nutritional, psycho-emotional) aspects, on the other hand, it is detrimental to the patients the postponement of surgery in order to capitalize on the multidisciplinarity of the given concept.

Another factor that would distort the concept of prehabilitation would be the heterogeneity of surgery, each with its specificity, which would broaden the criteria for inclusion/exclusion of patients who may or may not benefit from these programs. We have a business with patients physically compromised, weakened, immobilized, unstable psychically that we cannot associate with a prehabilitation program. Hence for the individualization of any type of treatment according to the patient's physio-pathogenetic specificity, it must also be applied to the concept, because not each patient is able to follow a multimodal prehabilitation program. As previously mentioned, patients with associated pathologies must benefit from an activity plan according to their somatic status, and be rigorously monitored throughout the program by the medical team to halt the precipitation of these risk factors.

The efficacy of the concept of prehabilitation is a controversial subject, also like its optimal duration, multiple studies contouring the interdependence of given aspects. In addition to the fact that prehabilitation can hurry the postoperative rehabilitation process, it has the potential to improve the quality of life and tolerance to neoadjuvant treatments such as chemotherapy [12].

Goals and objectives. The systematic literature review aims to study the effectiveness of the concept of prehabilitation and its influence on the functional parameters, the postoperative complications, and the quality of life of patients.

Material and methods. The Review Protocol followed the recommended methods by 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 and rcpjournals.org for relevant clinical studies in English for the last 6 years (August 2015 – July 2020) including all types of surgery. Searching strategy included the following key words: „prehabilitation", „preoperative exercises", „postoperative complications", „major surgery", „functional parameters".

Study settings

Criteria of inclusion: in extenso, year 2015–2020, more than 25 patients in study.

Criteria of exclusion: duplicated articles, without numerical parameters, less than 25 patients in study.

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 results of search in the mentioned databases identified 417 potential eligible citations, published between August 2015 and July 2020. After excluding the studies that were repeated (n=54) or that did not match with the topic of searching by title or by

abstract (n=331), 32 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 included clinical studies was assessed by Delphi criteria list [14]. Table 1 summarizes the assessment of the methodological quality of the 10 selected clinical trials. All studies had specified patient eligibility criteria. Only one study [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 evaluated the effectiveness of prehabilitation programs and recorded pre- and postoperative parameters. These were published between August 2015 and July 2020. A total of 939 patients were included in the studies. The size of the groups varied between n=26 and n=171, with an average of about 36 patients. The studied surgical populations were as follows: elective thoracotomies [15, 16, 17, 18, 23], gastric resection [19], aortocoronary bypass [20], colorectal resection [21], spinal surgery [22], pancreatoduodenectomy [24].

Mark L. (2016) [15] in a prospective study, on 151 patients, hypothesized that a high-intensity interval training (HIIT) program, could improve the functionality of the cardio-respiratory system before 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).

Maximal cardiopulmonary exercise testing and the six-minute walk test were performed twice before surgery. The primary outcome measure was a composite of death and in-hospital postoperative complications. The primary endpoint did not differ significantly between the two groups: 27 of the 74 patients (35.5%) in the PG and 39 of 77 patients (50.6%) in the CG group developed at least one postoperative complication (P=0.080). Noteworthy, the incidence of pulmonary complications was lower in the PG compared with the CG group (23% vs 44%, P=0.018), owing to a significant reduction in

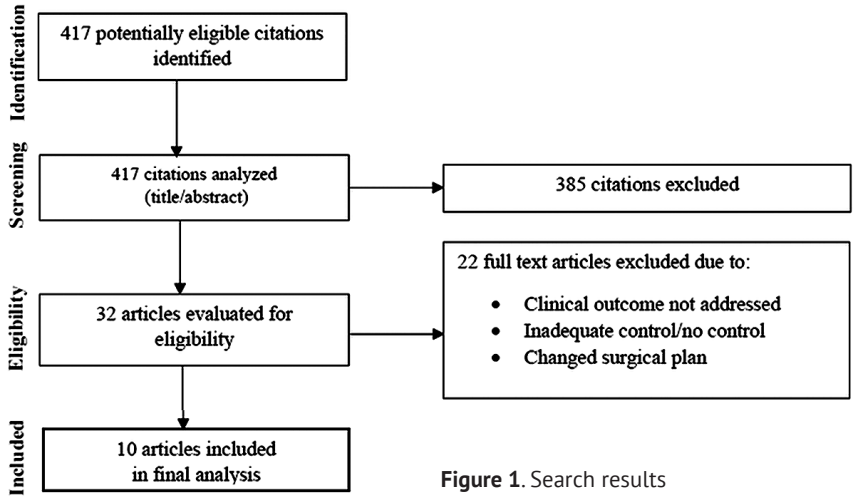

Figure 1. Search results

Table 1

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

Clinical trial	Randomized?	Blind treatment allocation?	Baseline similar groups?	Specified eligibility criteria?	Blinded outcome assessors?	Patient blinded?	Medical provider care blinded?	Assessing the variability of the primary outcome?	Study includes an intention-to treat analysis?	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
Enrico M. (2017) [19]	Yes	No	Yes	Yes	No	No	No	Yes	Yes	5/9
Steinmetz C. (2020) [20]	Yes	No	Yes	Yes	No	No	No	Yes	Yes	5/9
Annefleur E. (2018) [21]	Yes	No	Yes	Yes	No	No	No	Yes	Yes	5/9
Marchand A. (2019) [22]	Yes	No	Yes	Yes	No	No	No	Yes	Yes	5/9
Boujibar F. (2018) [23]	Yes	No	No	Yes	No	No	No	Yes	Yes	4/9
Ausania F. (2019) [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.

atelectasis (12.2% vs 36.4%, P<0.001), and this was accompanied by a shorter length of stay in the post-anesthesia care unit (median –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 home prehabilitation program on functional capacity of lung in patients that suffer from cancer, subjected to VATS lobectomy. CG consisted of 36 patients, and PG of 37 patients who benefited preoperatively from a 2-week prehabilitation program. The value of 6MWD was 60.9 m higher perioperatively in PG compared to CG (95% CI [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 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 resectable lung cancer. Of 342 potential lung cancer cases, 142 high-risk patients were finally divided into two groups: PG (n = 71) underwent

Table 2

Characteristics of the analyzed studies

Author Year Reference	Type of surgery	Applied prehabilitation elements	Recorded parameters
Marc Licker (2016) [15] n= 151	LR (LE, PE) OT VATS	H – MIIT	*Preoperatively:* VO_2 max; 6MWT; CPET *Postoperatively:* POC; Length of hospital stay; Mortality
Zijia Liu (2020) [16] n=73	LR VATS	Aerobic Endurance exercises Breathing exercises Nutrition counseling with whey protein supplementation Psycho-emotional guidance Meditation	Preoperatively: 6MWT; 6MWD; Evaluation of lung function; Assessment of the degree of disability; Psychometric evaluation *Postoperatively:* Quality of short-term recovery; Length of hospital stay; POC; Mortality
Laurent H. (2020) [17] n=26	LR (LE; PE) VATS OT	Respiratory muscle endurance exercises	*Preoperatively:* Evaluation of lung function (EV, VO_2 max), ET *Postoperatively:* POC (Clavien-Dindo classification); Length of hospital stay; Mortality
Gao et al. (2015) [18] n=142	LR (LE) VATS OT	Abdominal breathing exercises volumetric devices (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	*Preoperatively:* Evaluation of lung function; CPET *Postoperatively:* POC (pneumothorax, subcutaneous emphysema, diarrhea, allergic reactions, arrhythmias, lung infection); Length of hospital stay; The cost of rehabilitation
Enrico M. (2017) [19] n=68	GR	Physical exercises aerobic Nutritional diet	*Preoperatively:* 6MWD *Postoperatively:* POC; Length of hospital stay
Steinmetz C. (2020) [20] n=171	Coronary bypass	Aerobic exercises Exercises on the bike Balance exercises	*Preoperatively:* 6MWD; CPET *Postoperatively:* 6MWD; POC
Anael B. (2018) [21] n=125	Major abdominal surgeries	H-MIIT Endurance exercises Nutritional counseling	*Preoperatively:* CPET; Aerobic capacity *Postoperatively:* POC; Mortality

Continuation of the Table 2

Author Year Reference	Type of surgery	Applied prehabilitation elements	Recorded parameters
Marchand A. (2019) [22] n= 97	SS	Aerobic exercises Spinal stabilization exercises	*Preoperatively:* The intensity of low back pain; Lumbar disability; Elasticity of the spine *Postoperatively:* Quality of life; POC
Boujibar F. (2018) [23] n=38	LR VATS RATS	Physical exercises Breathing exercises Smoking cessation	*Preoperatively:* Evaluation of lung function; CPET *Postoperatively:* POC; Mortality
Ausania F. (2019) [24] n=48	PDE	Physical exercises Breathing exercises Nutritional diet Enzymatic supplement	*Preoperatively:* Spirometry; Pulse oximetry; 6MWT; Anthropometry *Postoperatively:* POC (Clavien-Dindo classification)

LR – Lung resection; LE – lobectomy; PE – pulmonectomy, VATS – Video-assisted thoracoscopic surgery; OT – Open thoracotomy, GR- Gastric resection; SS- Spine surgery; RATS – Robotic-assisted thoracoscopic surgery; PDE – pancreatoduodenectomy; CPET- Cardiopulmonary exercise testing, 6MWT – 6 minutes walk test; 6MWD – 6 minutes walking distance, H-MIIT – high-intensity interval training, POC – Postoperative complications; EV – Expiratory volume; ET – Endurance time

an intensive pre-operative pulmonary prehabilitation program, followed by lobectomy; group CG (n = 71) underwent only lobectomy with conventional management. Postoperative complications, average days in hospital, postoperative days in hospital, and cost were analyzed.

The rate of postoperative total complications in PG (16.90%) was significantly lower than in group CG (83.31%) (P = 0.00), as was the rate of postoperative pulmonary complications PPC: PG (12.81%) *versus* CG (13.55%) (P = 0.009); the PPC in the left lung (17.9%) was higher than in the right lung (2.3%) (P = 0.00). The average days in hospital in group S was significantly higher than in group R (P = 0.03). There was no difference between groups in average hospital cost (P = 0.304).

Enrico M. (2017) [19] developed a randomized clinical trial (available-case analysis based on completed assessments), targeting 68 patients. The study was conducted at McGill University Health Centre (Montreal, Quebec, Canada) comparing prehabilitation with a control group. Intervention consisted of preoperative exercise and nutrition optimization. Participants were adults awaiting elective esophagogastric resection for cancer. Preoperative (end of the prehabilitation period) and postoperative (from 4 to 8 weeks after surgery) data were compared between groups. Compared with the control group, the prehabilitation group had improved functional capacity both before surgery (6MWD change, 36.9 [51.4] vs −22.8 [52.5] m; P < 0.001) and after surgery (6MWD change, 15.4 [65.6] vs −81.8 [87.0]m; P < 0.001).

Steinmetz C. (2020) [20] in a prospective study of 171 patients, had determined the impact of an exercise-based prehabilitation program on pre and postoperative exercise

Table 3

Results of the analyzed clinical studies

Author Year Reference	Main outcomes	Conclusions
Marc Licker (2016) [15] n= 151	*No significant differences between groups:* Postoperative complications (35.5% in PG, 50.6% in CG), P = 0.080, length of hospital stay (9 versus 10 days), P = 0.080 *Significant differences between groups:* VO_2max (+15% in PG, -8% in CG), P= 0.003 6MWT (+ 15% in PG, -8% in CG), P <0.001 CPET (+ 8% in PG), P = 0.005	As a matter of fact, the short-term intensive training program's safety and effectiveness have been demonstrated. However, compared to standard care, the targeted improvements failed to produce significant differences in morbidity-mortality rates.
Zijia Liu (2020) [16] n=73	*No significant differences between groups:* FEV1, postoperative complications, length of hospital stay *Significant differences between groups:* 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% Cl, 0.05–0.66; P = 0.021) VEM (L/min) (+19.8 (−21.0 vs 61.2) P = 0.339	This is the first randomized controlled trial of a multimodal prehabilitation program that combines aerobic exercise with physical endurance, breathing exercises, nutrition, and psychological support. Despite the limitations of the study, the authors were able to demonstrate the program's effectiveness in increasing the values of parameters such as 6MWD, FVC, and VEM).
Laurent H. (2020) [17] n=26	*No significant differences between groups:* Length of hospital stay, VO_2 max. *Significant differences between groups:* Postoperative pulmonary complications (2 vs. 10, P = 0.037) VE and ET increased only in LP (+ 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 și col. (2015) [18] n=142	*No significant differences between group:* CPET, FEV1, cost of hospitalization (no difference) *Significant differences between group:* Postoperative complications (16.9% in PG and 83.3% in CG), P = 0.00 Length of hospital stay (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 pre-rehabilitation program was demonstrated, which decreased the complication rate in PG compared to CG.
Enrico M. (2017) [19] n=68	*No significant differences between groups:* Number and severity of complications, length of hospital stay *Significant differences between groups:* 6MWD preoperative – (36.9 [51.4] min in PG + 62% vs −22.8 [52.5] m in CG;P <0.001) 6MWD postoperatively -15.4 [65.6] min in PG vs −81.8 [87.0] min in CG; P <0.001)	Patients undergoing surgery for malignant lesions of the gastroesophageal tract had a substantial increase in health during prehabilitation, according to this randomized clinical trial. However, further investigations are needed to determine the optimal modality of the pre-rehabilitation program and its effect on the overall oncological results.

Continuation of the Table 3

Author Year Reference	Main outcomes	Conclusions
Steinmetz C. (2020) [20] n=171	*No significant differences between groups:* CPET, postoperative complications *Significant differences between groups:* 6MWD preoperatively (PG: Δ + 50.5 m, P <0.001; LC: Δ + 14.2 m, P <0.001; P = 0.003) 6MWD immediately postoperatively (LP: Δ – 64.7 m; CG: Δ – 100.8 m; P = 0.013) 6MWD after cardiac rehabilitation (PG: Δ + 47.2 m; CG: Δ + 5.7 m; P <0.001) Quality of life (PG: Δ0.3–0.4, P ≤ 0.001; control group: Δ0–0.1; P ≤ 0.001; P <0.001)	In conclusion, the resistance exercises derived from the prehabilitation program implemented in the study targeting patients with cardiac pathology, proved to be harmless and effective in raising the quality of life of these patients and improving 6MWD parameters both preoperatively, postoperatively immediately, and late).
Anael B. (2018) [21] n=125	*No significant differences between groups:* CPET *Significant differences between groups:* Aerobic capacity [ΔET 135 (218) %; P <0.001) Postoperative complications (31% vs 62% (RR 0.5; 95% CI, 0.3–0.8; P = 0.001)	The pre-rehabilitation improved the postoperative clinical results of the candidates for major elective abdominal surgery, this success can be explained by the increase of the preoperative aerobic capacity of these patients.
Marchand A. (2019) [22] n= 97	*No significant differences between groups:* Length of hospital stay, postoperative complications, intensity of low back pain, elasticity of the spine *Significant differences between groups:* Quality of life after intervention (83.7% ± 25.9 in PG and 80% ± 25.3 in CG (p = 0.68)	Finally, the safety of the pre-rehabilitation program in surgical patients was demonstrated. Significant outcomes are limited to postoperative patient feedback.
Boujibar F. (2018) [23] n=38	*No significant differences between groups:* CPET, FEV1, length of hospital stay (no difference) P = 0.644 *Significant differences between groups:* 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.
Ausania F. (2019) [24] n=48	*No significant differences between groups:* Postoperative complications (54.5% vs 33.3%, respectively; p = 0.18) *Significant differences between groups:* FVC (+ 20%), SpO_2 (+ 20%) Dynamometry + 16% on the right hand, + 21% on the left hand, 6MWT – +19%	This study was unable to demonstrate the benefit of a pre-rehabilitation program for patients undergoing pan-creatoduodenectomy with certainty. Increasing the recorded parameter values had no significant effect on postoperative complications.

PG – Prehabilitation group; CG – Control group, SpO_2 – Oxygen saturation EV – Expiratory volume; ET – Endurance time; RR – Relative risk; CI – Confidence interval

capacity, functional capacity, and quality of life in patients awaiting elective coronary artery bypass graft surgery.

A total of 171 patients (PG, n = 81; CG, n = 90) completed the study. Functional capacity (6MWD: 443.0 ± 80.1 m to 493.5 ± 75.5 m, P = 0.003) and quality of life (PG: 5.1 ± 0.9 to 5.4 ± 0.9, P <0.001) increased relatively more in PG compared to CG during preoperative period.

Annefleur E. (2018) [21] conducted a prospective randomized study targeting 125 patients undergoing major abdominal surgery. The author states that the prehabilitation program can improve the cardiorespiratory functionality of patients, it remains to be seen whether prehabilitation also reduces postoperative complications, as most of the studies so far were rather underpowered, heterogeneous, and biased toward the selection of patients with a lower risk of postoperative complications. After 19 patients were excluded, due to the change of the surgery plan, 63 patients underwent analysis at CG and 62 at PG. The program managed to increase the aerobic capacity of patients, reduce the number of patients who suffered postoperative complications by 51% (RR 0.5; 95% CI, 0.3–0.8; P = 0.001) and minimize the rate of postoperative complications in PG compared to CG.

Marchand A. (2019) [22] in his study of 97 patients intends to evaluate the feasibility of conducting a preoperative intervention program in patients with lumbar spinal stenosis and report the results of the proposed intervention. One group of patients (N = 48) was attached to a supervised preoperative prehabilitation program for 6 weeks and another group (N = 49) represented the control group. Results were measured at the start of the program, 6 weeks later, and again 6 weeks, 3 months, and 6 months after surgery. This study showed significant differences between groups only in terms of quality of life (83.7% ± 25.9 in PG and 80% ± 25.3 in CG (P = 0.68). The absence of adverse reactions, correlated with positive changes observed in the results recorded in PG, justifies the initiative of conducting a large-scale study to evaluate the effectiveness of the given program.

Boujibar et al. (2018) [23] reported their results in a study to determine whether participation in a prehabilitation program would improve outcomes after surgery and decrease morbidity according to the Clavien-Dindo classification. The cohort included 38 patients. Two groups were formed: one group with prehabilitation (n=19) and one group without prehabilitation (n=19). Four patients were not included leaving 34 patients for the final analysis. Most patients with a Clavien-Dindo grade of ≤2 had received prehabilitation compared to patients who had not received prehabilitation, respectively 17/19 *vs.* 8/15; P=0.0252. Patients who had received prehabilitation had fewer postoperative complications than patients who had not received the prehabilitation program, respectively 8/19 *vs.* 12/15; P=0.0382.

Ausania F. (2019) [24] in a study of 48 patients, tried to demonstrate the positive impact of prehabilitation in reducing the incidence of postoperative complications in patients with pancreatic or periampullary tumors to undergo pancreatoduodenectomy. No statistically significant differences were identified in the incidence of postoperative complications between the 2 groups (PG and CG). The present study did not notice significant differences between groups in the presence of pancreatic fistulas (11% vs 27%, p = 0.204). However, the increase in FVC (+ 20%) and SpO_2 (+ 20%) values was demonstrated.

In 2/10 studies high-intensity interval training was applied [15, 21], in 4/10 aerobic exercises [16, 19, 20, 22], and in 5/10 studies breathing exercises were taken in the pre-

habilitation program [16, 17, 18, 23, 24]. Smoking cessation was applied in 2/10 studies [18, 23] and nutritional counseling in 4/10 studies [16, 19, 21, 24]. Drug therapy (antibiotics, bronchodilators, expectorants, corticosteroids) was implemented only in the study of Gao et al. [18].

In 2/10 studies a monodisciplinary prehabilitation program was chosen [15, 17], in 8/10 multidisciplinary was valued [16, 18, 19, 20, 21, 22, 23, 24]. The duration of the program varied as follows: 7 days [18, 23], 14 days [16, 20], 21 days [17], 25 days [15], 30 days [19], and in 4/10 studies the longevity of the program was not mentioned.

All 10 studies recorded the parameters before the beginning of the program, pre- and subsequently postoperatively. In Marchand A.'s study [22] the results were recorded both preoperatively, immediately postoperatively, and late postoperatively (6 weeks, 3 months, and 6 months after the 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 achieved in the 10 studies were divided into two categories: no significant differences between groups and significant differences between groups. Consequently, 4/10 studies recorded significant differences between batches of the *6MWD* parameter (6 minutes walking distance) [15, 16, 19, 20]. Steinmetz C. et al. [20] demonstrated that endurance exercises derived from the prehabilitation program implemented in the study, targeting patients with heart disease, proved to be harmless and effective in raising the quality of life of these patients and improving 6MWD parameters both preoperatively, immediate and late postoperative. It should be noted that the study by Mark L. [15] where was preferred a program that includes only H-MIIT (high-intensity-moderate-intensity physical training) compared to other studies [16, 19, 20] that addressed patients multidisciplinary, has achieved promising results of the 6MWD parameter.

The *CPET* (cardiopulmonary exercise testing) parameters were processed in 5/10 studies [15, 18, 20, 21, 23], of which in 4/10 no significant differences were found between groups [18, 20, 21, 23]. Significant differences between batches of CPET parameters can be noted in the prospective study of Mark L. [15].

Studies tend to initiate an encouraging vibration regarding *respiratory parameters*, such as VO_2 max, FVC, VEM, VE, and ET. In 4/10 studies, significant differences were registered between groups in terms of respiratory functional explorations [15, 16, 17, 24]. Mark L. [15] and Zijia Liu [16] have shown relevance to this topic, the latter one succeeding through a multimodal program to demonstrate the effectiveness of the prehabilitation program in increasing the values of parameters such as 6MWD, FVC, and VEMS. The research by Laurent H. [17] was limited to a total of 26 patients in both groups, and larger groups might be needed to reveal the effects of the prehabilitation program on functional parameters.

In terms of the criterion of *hospitalization period*, only 1 of 7 studies [15, 16, 17, 18, 19, 22, 23] that addressed this parameter found substantial differences between groups in the given subject [18]. The analyzed studies also failed to demonstrate the impact of the prehabilitation program on *lowering the cost* of these patients' hospitalization (parameter interdependent with the period of hospitalization of patients).

The effect of the focused program on reducing *postoperative complications* in pacients is of specific and significant importance. This criterion was analyzed in 10/10 studies, but only 4/10 studies [17, 18, 21, 23] managed to demonstrate the effectiveness of the prehabilitation program. Laurent H. [17] discovered a significant increase in muscular endurance in the prehabilitation group compared to the control group, which was associated with a markedly decreased number of postoperative pulmonary complications. Gao et al. [8] revealed that their efforts were not in vain, as they obtained positive postoperative complications outcomes (16.9 % in PG and 83.3 % in CG). Anael B. [21] managed to improve the postoperative clinical outcomes (postoperative complications: 31% in LP and 62% in LC) of candidates for major elective abdominal surgery in her study. According to the findings of the Boujibar F. [23] study, prehabilitation has a positive impact on the occurrence and severity of postoperative complications (42% in PG, 80 % in CG).

An extra possibility/perspective offers the subtle criterion that encompasses the quality of life of these patients after surgery. Even if this parameter was mentioned in only one study [23], because it was the only extended study with late postoperative results, this criterion is a special goal of clinicians and should not be overlooked.

Discussion. This systematized literature review identified the heterogeneity of prehabilitation programs for patients undergoing large-scale surgeries in terms of composition, duration, mode of administration, and specificity of the results obtained that quantify their impact. All of these are critical elements that must be standardized in future evaluations of the impact of prehabilitation on short- and long-term outcomes in this patient population.

Prehabilitation is a promising paradigm. Conceptually intuitive, and based on sound theoretical principles, the emerging evidence is encouraging. Even so, we are yet to establish how best to utilize this tool, which combination of interventions is the most effective, whether they need to be tailored to the type of surgery to be performed, and whether prehabilitation, on the whole, is cost-effective [25].

The American College of Sports Medicine clearly states in its guidelines for cancer survivors that exercise is safe in the pre-operative and post-operative periods, and leads to improved physical functioning and better quality of life [26]. What is certain is that prehabilitation was completely safe for the patients in the study groups. However, since only one study out of the ten analyzed in this review found significant differences between groups, little evidence has been documented in favor of the major impact of the prehabilitation concept on the reduction of postoperative complications.

The value of the concept of prehabilitation is empirically demonstrated in thoracic surgery, where progress in lung function parameters becomes critical for patients undergoing such interventions. Major surgery induces a high systemic inflammatory response associated with a marked increase in oxygen consumption in the immediate postoperative period [27, 28]. Inpatients with poor cardiorespiratory reserve, the inability to sustain this increased demand may lead to avoidable morbidity and mortality [29]. The amplification of the values (FEV_1, VO_2 max, EV, FVC) can contribute if not to the avoidance, then at least to the improvement of the severity of the postoperative complications, as well as to the catalysis of the rehabilitation process. At the beginning of this century, in a relatively short period of time, pulmonary rehabilitation has become recognized as a cornerstone in the management of patients with COPD [30].

The issue of program longevity, which appears to be directly proportional to the dynamism of the patients in the prehabilitation group, is of significant importance. This is a topic that should be researched prospectively, with a larger number of patients.

Another challenge to which the study was subjected was to maintain adherence to the program, even though the human factor became known. Some patients were distinguished by marked deconditioning, and others by an essential sedentary level. Adherence is a major limitation in any study using exercise as an intervention. It is imperative to have an enjoyable exercise protocol, especially because waiting for a potentially lifesaving operation is very stressful. Several studies are suggesting that HIIT is perceived to be more pleasurable even if it is more physically demanding than a moderate-intensity exercise regime [31–34]. This is supported by Mark L.'s [15] study, which demonstrated that their program, which was entirely based on HIIT, was not only effective in increasing the values of functional tests but also had a high level of adherence.

The present study predisposes to questions whose answers are at least obvious: Does the given analysis offer the possibility of implementation and subsequent realization of the project? -Yes; Convincing enough? -Not.

Conclusions. Consequently, the concept of prehabilitation that includes exercise, psychological support and nutritional counseling is an essential adjuvant measure in major surgery. Prehabilitation can also be useful in selecting/sorting patients to undergo major surgery.

The issue is that the surgical society is currently faced with an insidious challenge that oscillates between two aspects of equal weight: we deal with patients who require time for prehabilitation, but the clinical dimension of oncology does not provide this time.

It has been proven that prehabilitation is not a retrograde concept, but it does not confirm that it can be progressive in this context. The lack of evidence suspends clinicians' enthusiasm to postpone the intervention in order to capitalize on the concept of prehabilitation.

Large-scale, high-quality studies are required to confirm the early evidence's promise and to determine the frequency, intensity, and duration of prehabilitation required to achieve optimal results.

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