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Predictive indicators of preoperative physical fitness on the incidence of cardiopulmonary complications after abdominal and non-cardiac thoracic surgery: a meta-analysis

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ABSTRACT

Pre-surgery physical fitness has proved to be lower in patients in patients with postoperative cardiopulmonary complications (PCPC) after thoracic and abdominal surgery. This meta-analysis summarised the risk estimates of PCPC for the various components of preoperative physical fitness. After a systematic search of medical databases, fourteen prospective cohort studies were included. Maximal aerobic capacity (VO_{2max}) was the most frequently studied component (n=10) besides stair climb test (n=3) and a two-minutes-exercise test (n=1). Twelve studies reported on lung surgery, one on abdominal surgery and one on both types of surgery. Eight studies reported on PCPC, three on postoperative pulmonary complications (PPC) and three on both complications. The pooled odds ratios (random model) for the risk of PCPC were 4.9 (95% CI 1.8–13.7) and 2.5 (95% CI 0.6–9.9) for $VO_{2max} < 15$ ml/kg/min and $VO_{2max} < 20$ ml/kg/min, respectively. Heterogeneity of results for $VO_{2max} < 15$ ml/kg/min were explained by methodological quality and degree of fitness of the study population. The pooled odds ratios (random model) for the risk of PPC were 2.7 (95% CI 0.4 –18.0) and 2.0 (95% CI 0.9–4.6) for $VO_{2max} < 15$ ml/kg/min and $VO_{2max} < 20$ ml/kg/min, respectively. The pooled odds ratio (fixed model) for inability of climbing three flight of stairs was 2.1 (95% CI 1.2–3.7). We conclude that physical fitness, expressed as VO_{2max} , is predictive for the development of PCPC in patients after lung surgery. More needs to be learned about the role of physical fitness in the outcomes of patients who undergo abdominal surgery.

INTRODUCTION

Cardiopulmonary complications are common after thoracic and abdominal surgery¹⁻³ and are a major cause of mortality, morbidity, prolonged hospital stay, and increased medical consumption.^{4,5} Several surgery- and patient-specific factors are known to increase the risk of postoperative complications, such as location of the incision in relation to the diaphragm and the type of anaesthesia used,⁶ older age (>60 years), and history of chronic obstructive pulmonary disease (COPD) and smoking.^{5,7,8} More recently, pre-surgery physical fitness has also been identified as major predictor of postoperative cardiopulmonary complications. Poor physical fitness affects the ability of a person to cope with hospitalization and surgery⁹ and may compromise postoperative functional recovery, potentially leading to postoperative complications.¹⁰⁻¹² Physical fitness is an integrated measure and includes several components, such as cardiorespiratory fitness and muscle function,¹³ and can be measured in different ways. Knowledge of those aspects of physical fitness that are associated with the incidence of postoperative complications could help improve the quality and efficiency of the outpatient preoperative screening procedure.

A meta-analysis by Benzo et al. revealed cardiorespiratory fitness, expressed as maximal oxygen consumption (VO_{2max} in ml/kg/min), to be significantly lower in patients who developed clinically relevant cardiopulmonary complications after lung surgery compared with patients without complications.¹⁴ This highlights the importance of VO_{2max} measurements to clinical decision-making and perioperative care in these patients. In practice, a maximal exercise test to exhaustion to assess cardiorespiratory fitness is expensive and a major burden for patients just before an operation, and especially for older patients. This raises the question whether maximal tests are always necessary and desirable – perhaps they could be replaced by more cost-effective submaximal tests. The meta-analysis by Benzo et al. reported differences in VO_{2max} between patients with or without complications, whereas in clinical practice a cut-off value is needed to identify patients at risk of cardiopulmonary complications. To address these issues, this meta-analysis includes submaximal exercise tests to estimate patients' physical fitness and focuses on risk estimates. The study is not restricted to lung surgery but also includes other types of non-cardiac thoracic surgery and abdominal surgery, with a view to establishing the predictive value of preoperative physical fitness for the risk of cardiopulmonary complications after abdominal and non-cardiac thoracic surgery.

METHODS

A systematic literature search was performed in the electronic databases MEDLINE, Embase, The Cochrane Database of Systematic Reviews, The Cochrane Central Register of Controlled Trials and CINAHL until December 2011.

Inclusion criteria were as follows:

- Study design: longitudinal prospective study design.
- Patients: adults (>18 years old) undergoing non-cardiac thoracic or abdominal surgery.
- Independent variables: studies investigating indicators of preoperative physical fitness and activity, e.g. muscle strength, aerobic/anaerobic exercise capacity, physical function testing, and activity level.
- Outcome variables: postoperative cardiopulmonary complications consisting of arrhythmia, myocardial infarction, heart failure, and pulmonary embolism; and postoperative pulmonary complications (classified according to the criteria of Kroenke^{15,16}).
- Data analysis: studies providing risk estimates for postoperative cardiopulmonary or pulmonary complications.
- Studies published in English.

Exclusion criteria were as follows:

- Patients undergoing cardiac, urological, gynaecological, paediatric, video-assisted thoracoscopic (VATS) surgery, or organ transplantation surgery.

The reference lists of retrieved articles, including review articles, were also searched for relevant articles. Titles and abstracts were first screened by two independent assessors (L.A.T. and E.W.S.). If the two assessors could not reach agreement, a third assessor (J.J.D.) made the final decision whether to include or exclude the study.

The methodological quality of observational studies was determined by two independent assessors (L.A.T. and E.W.S.), using the STROBE statement.²³ The level of agreement was represented by Cohen's kappa. The maximum Strobe score is 34 points: articles with a Strobe score of 24 or higher (>70%) were considered to be of 'high methodological quality', articles with scores between 17 and 23 (50–70%) were considered to be of 'moderate methodological quality', and articles with scores below 17 (<50%) were considered to be of 'low methodological quality'. Then the type of study, number of participants, surgical

procedures, complications (subgroups), complication rate, and preoperative risk factors, including physical fitness, were recorded.

Studies that were clinically homogeneous regarding postoperative complications and components of physical fitness were included in the meta-analysis, which was performed using the Comprehensive Meta-Analysis Program (CMA, version 2.2.064). Heterogeneity was assessed with the Cochrane Q statistic and calculation of an I^2 value with thresholds for low (25%–49%), moderate (50%–74%), and high (>75%) levels of heterogeneity. Random effect models were used when heterogeneity was present ($I^2 > 25\%$); otherwise fixed effect models were used. Existing heterogeneity was examined by meta-regression of the following categorized variables: age, physical fitness of the study population, methodological quality, and publication year. Significant variables ($p < 0.05$) were used for subgroup analysis.

RESULTS

The literature search identified 452 articles. After removal of duplicates and clearly irrelevant articles, 412 abstracts were reviewed, of which 361 were excluded. Four relevant articles were identified from the reference lists. Of the 55 potentially eligible articles, 41 were excluded after the full text was read, mainly because of methodological issues (e.g. retrospective studies) or non-applicable independent variable (i.e. physical fitness not used). Two studies were rejected because they were written in a language other than English (Chinese and Lithuanian). This resulted in 14 studies meeting the inclusion and exclusion criteria (see Figure 2.1).

Cardiorespiratory fitness expressed as maximal aerobic capacity (VO_{2max} , VO_{2peak} , percentage of predicted VO_{2max} and peak work rate) was the most investigated indicator of physical fitness ($n=10$),¹⁷⁻²⁶ followed by ability to perform a stair climb test ($n=3$)²⁷⁻²⁹ and a 2-minute exercise test ($n=1$).³⁰ Eight studies provided data on postoperative cardiopulmonary complications,^{19,20,23,24,26,27,29,30} three studies data on postoperative pulmonary complications,^{18,25,28} and three studies data on both complications.^{17,21,22} Twelve studies involved lung surgery,^{17-21,23-29} one abdominal surgery,²² and one abdominal and thoracic surgery.³⁰ Eight studies were of good^{18,19,23,25-28,30} and six were of low methodological quality.^{17,20-22,24,29} Level of agreement in assessing the methodological quality (Cohen's kappa) was .86 ($p < 0.05$). Table 2.1 summarizes the results of the included studies.

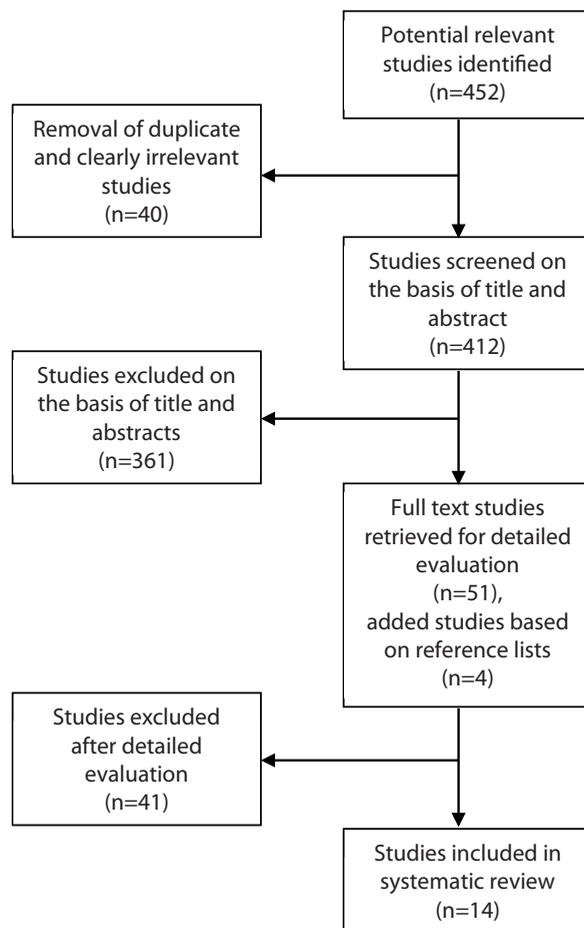


Figure 2.1 Flow chart of included articles.

All studies using a cut-off point of 15 and 20 mL/kg/min for VO_{2max} were included in a meta-analysis for postoperative cardiopulmonary and postoperative pulmonary complications separately. The results of the meta-analysis for postoperative cardiopulmonary complications as outcome measure are shown in the forest plots in Figure 2.2. The overall effect sizes (odds ratio) for $VO_{2max} < 15$ mL/kg/min and $VO_{2max} < 20$ mL/kg/min were 4.9 and 2.5, respectively (see Figure 2.2). Both groups showed low to moderate heterogeneity. For studies using a cut-off point of 15 mL/kg/min, meta-regression analysis showed a significant relationship between the risk of postoperative cardiopulmonary complications

Table 2.1 Summary of studies presenting odds ratios for the risk of postoperative cardiopulmonary complications and postoperative pulmonary complications by physical fitness

Author Year	MQ	N	Age	Surgical procedures	Complication rate (major PPC)	Indicators physical fitness	Cut-off point	Odds ratio	95% CI	Sensitivity	Specificity	
Postoperative cardiopulmonary complications												
Bayram ¹⁷ 2007	21	55	59 (20–74)	Lung surgery p-b-l	35%	VO _{2max}	<15 mL/kg/min	2.1	0.7–6.7	63%	56%	
Brutsche ¹⁹ 2000	25	125	63 ± 11	Lung surgery p-b-l-w-s	25%	VO _{2max}	<15 mL/kg/min	8.1	2.7–24.4	35%	94%	
							<60% pred mL/kg/min	11.3	2.1–59.3	19%	98%	
							<90% pred mL/kg/min	4.2	1.6–10.8	74%	59%	
Dales ²⁰ 1993	19	46	n.a.	Lung surgery p-l-w-t	32%	VO _{2max}	<1250 mL/min	4.2	1.1–15.6	67%	68%	
							<80% pred mL/min	0.7	0.2–2.5	53%	39%	
Markos ²¹ 1989	23	55	63 (14–80)	Lung surgery p-b-l-t	17%	VO _{2peak}	<15 mL/kg/min	1.2	0.4–4.3	40%	65%	
							<20 mL/kg/min	1.7	0.4–7.2	80%	29%	
Nugent ²² 1998	21	36	72.2 (57–85)	Abdominal surgery Aortic repair	23%	VO _{2max}	<20 mL/kg/min	1.4	0.3–7.3	63%	45%	
Smith ²⁴ 1982	22	22	55.7 ± 9.2	Lung surgery p-l-w-t	32%	VO _{2max}	<15 mL/kg/min	35	2.6–475.3	71%	93%	
							<20 mL/kg/min	12.6	1.4–97.9	100%	67%	
Wang ²⁶ 2000	24	40	64 ± 10	Lung surgery b-l-w-s	33%	VO _{2max}	<15 mL/kg/min	11.1	2.9–46.6	58%	89%	

Table 2.1 continues on next page

Table 2.1 *Continued*

Author Year	MQ	N	Age	Surgical procedures	Complication rate (major PPC)	Indicators physical fitness	Cut-off point	Odds ratio	95%CI	Sensitivity	Specificity
Postoperative cardiopulmonary complications											
Brunelli ²⁷ 2008	24	640	66.7 ± 9.3	Lung surgery	23%	Stair climbing	<12 metre climbing	2.1	1.1–3.7	13%	93%
Pate ²⁹ 1996	22	11	63.6 ± 4.9	p-b-l-w-s Lung surgery	64%	Stair climbing	<22 metre climbing <3 flights stair (<11 metre climbing)	2.3 2.1	1.5–3.4 0.1–63.4	69% 14%	50% 100%
Gerson ³⁰ 1990	25	177	73	abdominal/ non-cardiac thoracic surgery	22%	Cycle exercise test	Unable to cycle>2 min and HR>99 bpm	7.8	2.8–22.2	42%	91%
Richter Larsen ²³ 1997	27	97	64.3±8.9 (38–80)	Lung surgery p-l-w-t	32%	Work rate	<70Watt	4.0	1.5–11.0	39%	86%
Postoperative pulmonary complications											
Bayram ¹⁷ 2007	21	55	59 (20–74)	Lung surgery p-b-l	20% (7%)	VO _{2max}	<15 mL/kg/min	36.1	2.0–653.0	100%	61%
Bobbio ¹⁸ 2009	25	73	66.7 ± 8.7	Lung surgery b-l-s	26% (19%)	VO _{2max}	<15 mL/kg/min <18.7 mL/kg/min <20 mL/kg/min	2.6 5.6 5.0	0.8–9.0 1.8–17.6 1.0–23.9	32% 52% 89%	85% 84% 37%

Author Year	MQ	N	Age	Surgical procedures	Complication rate (major PPC)	Indicators physical fitness	Cut-off point	Odds ratio	95%CI	Sensitivity	Specificity
Postoperative pulmonary complications											
Markos ²¹ 1989	23	55	63 (14–80)	Lung surgery p-b-l-t	17%	VO _{2peak}	<15 mL/kg/min <20 mL/kg/min	0.5 0.7	0.1–2.9 0.1–3.4	25% 63%	61% 30%
Nugent ²² 1998	21	36	72.2 (57–85)	abdominal Isurgery Aortic repair (10%)	13%	VO _{2max}	<20 mL/kg/min	0.7	0.1–6.0	50%	42%
Torchio ²⁵ 1998	24	54	62 ± 10.2	Lung surgery p-b-l-o	29% (5%)	VO _{2max}	<20 mL/kg/min	4.1	0.8–20.6	88%	37%
Girish ²⁸ 2001	24	83	67 39–84	abdominal/ non-cardiac thoracic surgery	25%	Stair climbing	<6 metre <10 metre <12 metre <15 metre	15 5.9 6.3 4.2	2.8–80.1 1.8–18.7 2.1–18.4 0.9–19.9	38% 48% 71% 95%	97% 90% 77% 32%
Gerson ³⁰ 1990	25	177	73	abdominal/ non-cardiac thoracic surgery	14%	Cycle exercise test	Unable to cycle>2 min and HR>99 bpm	7.1	23.2– 15.9	28%	95%

P, pneumectomy; l, lobectomy; bl, bilobectomy; s, segment resection; w, wedge resection; t, thoracotomy; o, other.

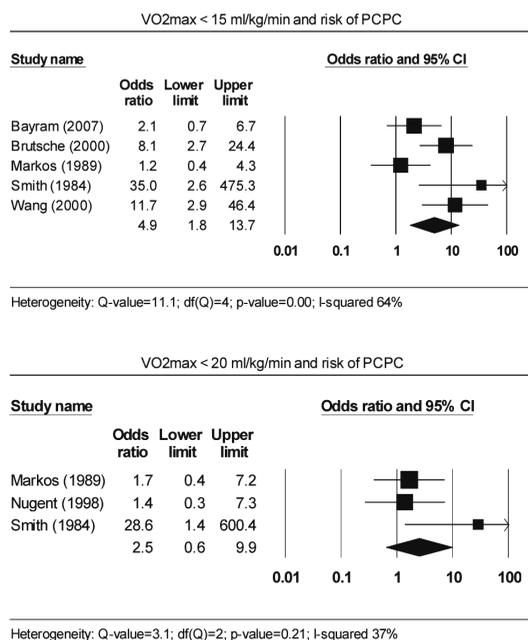


Figure 2.2 Forest plot of the odds ratios and 95% confidence intervals reported in studies of the association between VO_{2max} <15 mL/kg/min and <20 mL/kg/min and postoperative cardiopulmonary complications (PCPC) (random model).

(expressed as odds ratios) and the methodological quality of the studies and the degree of physical fitness (measured as the mean VO_{2max} of the total study population) (Figure 2.3), but not significant associations between the risk of these cardiopulmonary complications and age or publication year. Studies of high methodological quality revealed homogeneity and an overall odds ratio for postoperative cardiopulmonary complications of 9.3. The likelihood of cardiopulmonary complications was higher in studies including patients with a higher cardiopulmonary fitness (mean VO_{2max} of the total population >17.5 mL/kg/min) than in studies including patients with a lower cardiopulmonary fitness (odds ratio 10.6 versus 1.7, respectively; see Figure 2.3). The results for both groups showed homogeneity (I² 0%).

The results of the meta-analysis of four studies reporting on postoperative pulmonary complications are shown in the forest plots in Figure 2.4. The likelihood of pulmonary complications was similar in the groups with a low and high cardiopulmonary fitness

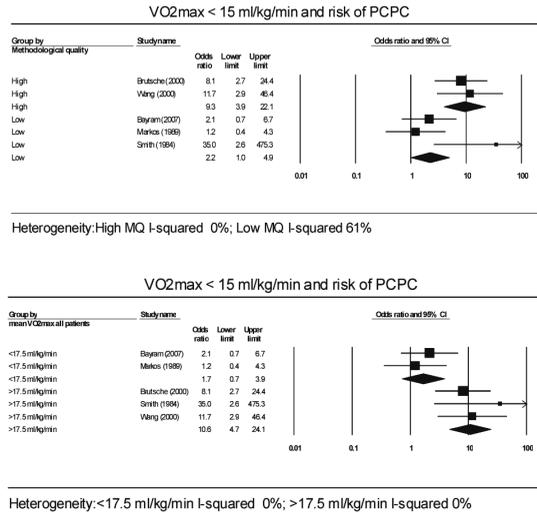


Figure 2.3 Forest plot of subgroup analysis of the effect of methodological quality and mean VO_{2max} of the total study population on the association between VO_{2max} < 15 mL/kg/min and postoperative cardiopulmonary complications (PCPC).

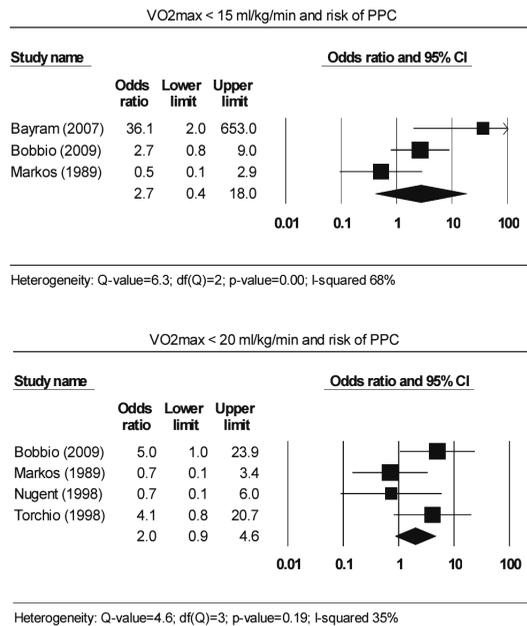


Figure 2.4 Forest plot of the odds ratios and 95% confidence intervals reported in studies of the association between VO_{2max} < 15 mL/kg/min and < 20 mL/kg/min and postoperative pulmonary complications (PPC) (random model).

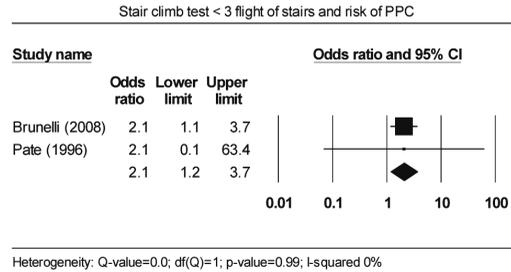


Figure 2.5 Forest plot of the odds ratios and 95% confidence intervals reported in studies of the association between the stair climb test (<3 flight of stairs) and postoperative cardiopulmonary complications (PCPC) (fixed model).

($VO_{2max} < 15$ and 20 mL/kg/min, respectively), with pooled odds ratios of 2.7 and 2.0 , respectively. Meta-regression analysis did not identify variables for subgroup analysis.

Two studies investigated physical fitness and the risk of postoperative cardiopulmonary complications using a stair climb test (<12 m or three flights). Both studies revealed a higher likelihood of complications (odds ratio 2.1) in patients who could not climb three flights of stairs (see Figure 2.5).

DISCUSSION

This meta-analysis provided evidence that poor physical fitness, defined as VO_{2max} of 15 mL/kg/min or lower or inability to climb three flights of stairs, is a predictor of cardiopulmonary complications after lung surgery (overall OR 4.9 and 2.1 , respectively). Physical fitness measured as VO_{2max} seemed to be a more robust predictor of cardiopulmonary complications than of pulmonary complications. The 15 mL/kg/min threshold provided a high specificity and low sensitivity (see Table 2.1), meaning that while the detection rate for patients ‘not at high risk’ is high, a substantial proportion of patients ‘at high risk’ are not detected. The opposite is true for the cut-off value of 20 mL/kg/min (see Table 2.1), which had a high detection rate for patients ‘at high risk’. This finding suggests that both cut-off values should be used. The high specificity of the 15 mL/kg/min cut-off value seems appropriate for deciding whether to operate (no wrong decision to withhold surgery) and the high sensitivity of the 20 mL/kg/min cut-off value is appropriate for screening and decisions about perioperative management (no wrong decision to withhold ‘high-risk’ treatment).

Although the current review was limited to cardiopulmonary complications, the results are in line with those reported by Colice et al.³¹ and Beckels et al.,¹⁶ who also included mortality as postoperative complication. Our recommendations about the use of the two cut-off points of VO_{2max} (15 and 20 mL/kg/min) are in agreement with theirs. Most studies have used the cut-off points of 15 and 20 mL/kg/min, as recommended in the literature. Two studies used ROC curve analysis to establish cut-off points, which were 15 mL/kg/min²⁶ and 18.7 mL/kg/min.¹⁸ A ROC curve analysis of all studies could further validate the recommended cut-off points, but only one study provided the original data²¹ required for this analysis.

Cardiopulmonary fitness expressed as VO_{2max} (mL/kg/min) may be biased by body weight; however, none of the included studies provided sufficient data to correct the results of the meta-analysis for weight (only one study expressed cardiopulmonary fitness as mL/kg).²⁰ The same applies to bias by age, which could be corrected by presenting the results as percentage of the predicted VO_{2max} , which takes age and gender into account (two studies presenting this unit of measurement made use of different cut-off points^{19,20}).

Besides VO_{2max} , the height climbed by patients on a stair climb test was the most commonly used measure of physical fitness. This test is considered a surrogate for the VO_{2max} and represents a low technology and more cost-effective exercise regimen.³² The current study provides evidence that patients who cannot climb three flights of stairs are at risk of postoperative cardiopulmonary complications; however, this result is based on just two studies and is dominated by one author. The value of the stair climb test may be improved by including the time it takes to climb the stairs, as indicated by a number of authors,³²⁻³⁴ especially as workload (as VO_{2max}) incorporates a measure of time (its unit is joules per second). This rationale argues for a test measuring the height climbed in 1 minute. In the study of Koegelenberg et al., cut-off points for a climbing speed of 12 m/min and 15 m/min were found to correspond with VO_{2max} cut-off points of 15 mL/kg/min and 20 mL/kg/min, respectively.³³ As weight will also influence performance on a stair climb test,³² both factors (time and body weight) should be taken into consideration in future studies.

Most of the meta-analyses yielded heterogeneous results. Subgroup analysis for different levels of physical fitness resulted in homogeneous effect sizes in studies in which the 15 mL/kg/min cut-off point was used for risk stratification. The studies that included fitter individuals (mean VO_{2max} of patients >17.5 mL/kg/min) reported higher odds ratios for postoperative complications than did studies with less fit participants (mean VO_{2max} <17.5 mL/kg/min; pooled odds ratio 10.6 and 1.7, respectively). This can be explained by smaller difference between patients at risk and not at risk for postoperative complications

in the latter group. The mean VO_{2max} for the patients not at risk for complications was 21.1 and 16.8 mL/kg/min for the fitter and less fit group, respectively. In other words, studies that include physically fit patients generate higher odds ratios. Clinicians should take this into account when interpreting the results of studies.

Although odds ratios are widely used, they are difficult to interpret. They are often considered to be equivalent to the relative risk. But this inaccuracy always entails overestimation of risk, which increases with the incidence of the dependent variable, in this study the postoperative complication rate. The high odds ratios in the studies of Smith et al.²⁴ and Bayram et al.¹⁷ (35 and 36, respectively) were because empty cells precluded the calculation of odds ratios with the inverse variance method. Adding 0.5 to each cell provides the usual solution for this problem,³⁵ but may give rise to high values. The Peto method is recommended for calculating odds ratios when empty cells occur³⁵ and reduced the risk to more reliable values. We did not use this method because it assumes effect ratios are close to unity and that there are similar numbers of individuals in the at-risk and not-at-risk groups.³⁶

Our search string identified 452 potentially relevant studies, to which 4 studies were added by checking the reference lists of full-text articles. This suggests that our search string was sensitive. Only 2 articles had to be excluded because they were published in a language other than English. As more than 90% of the studies reported on lung cancer surgery, our findings might not be directly transferable to abdominal surgery. Moreover, most of the studies were published before 2005, which raises questions about the validity of the results because surgery and anaesthesia techniques have changed over time; however, we did not find great differences in postoperative complication rates over the years. Recent studies investigated differences in physical fitness between patients who did, or did not experience complications,³⁷⁻⁴⁰ but these studies were excluded because they did not provide risk measures. They did report significantly lower levels of physical fitness in patients with cardiopulmonary complications, corroborating the importance of physical fitness.

Future research should investigate the effects of physical fitness on the postoperative course of patients scheduled for abdominal surgery, using a comprehensive measure of physical fitness and physical activity as proposed by Feeney.^{37,41} Physical fitness is a potentially modifiable factor even in older patients. Several researchers recommend a preoperative exercise programme ('prehabilitation') to improve patient outcomes after major thoracic or abdominal surgery.⁴²⁻⁴⁶ This experimental research should be expanded to further clarify the role of physical fitness.

In conclusion, our results suggest that physical fitness, expressed as VO_{2max} , is a strong predictor of the development of cardiopulmonary complications in patients after lung surgery. More needs to be learned about the role of physical fitness in the outcomes of patients who undergo abdominal surgery.

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