Postoperative Pulmonary Function in Open versus Laparoscopic Cholecystectomy: A Meta-Analysis of the Tiffenau Index

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Key Words

Open cholecystectomy · Laparoscopic cholecystectomy · Pulmonary function · Forced expiratory volume in 1 second · Forced vital capacity · Meta-analysis · Tiffenau Index

Abstract

Background: Available scientific literature about open cholecystectomy (OC) and laparoscopic cholecystectomy (LC) does not show univocal results in terms of postoperative pulmonary function. A meta-analysis was carried out to evaluate the postoperative pulmonary function after OC and LC focusing on the Tiffenau index. **Methods:** Electronic databases were consulted (Cochrane Library, Embase and Pubmed). Standardized mean difference (SMD) with 95% CI was calculated for the Tiffenau Index. The kappa test was performed to evaluate agreement between the reviewers regarding the quality of the selected studies. A sensitivity analysis was carried out to assess the robustness of our study. Heterogeneity among studies was tested by using a χ^2 test at 0.05 significance level. A random effects model meta-analysis was performed. **Results:** Meta-analysis of the 13 articles included, resulted in a SMD of 53% (95% CI 0.04, 1.02) for the Tiffenau Index in favor of laparoscopic cholecystec-

tomy. The χ^2 test analysis showed the presence of heterogeneity among studies (Tiffenau index $\chi^2 = 99.97$, $p = 0.03$). The sensitivity analysis confirms the validity of our results. **Conclusions:** Postoperative pulmonary function is better preserved after laparoscopic cholecystectomy than open cholecystectomy.

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Introduction

Cholecystectomy, surgical removal of the gallbladder, is one of the most common elective procedures performed by general surgeons [1].

Advanced laparoscopic technologies make it possible to remove the gallbladder through a tiny incision at the navel.

The speed with which laparoscopic cholecystectomy has been developed and introduced into routine practice is unprecedented in the history of surgical procedures. The introduction of laparoscopic cholecystectomy induced a significant growth in cholecystectomy rates [2, 3].

Laparoscopic cholecystectomy has quickly become a popular alternative to open cholecystectomy.

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Smaller incisions and the use of laparoscopic techniques allow substantial reductions in pulmonary function to be prevented postoperatively [4, 5].

Altogether, laparoscopy is considered a cost-effective technique for the therapy of symptomatic cholecystolithiasis [6, 7] showing a number of advantages over laparotomy.

In particular, regarding the dimension of the effectiveness, it is possible to distinguish two different kinds of outcome related to admission period: intra-admission and post-admission outcomes.

According to scientific literature, post-admission outcomes of laparoscopic cholecystectomy are faster return to normal activities and a better quality of life [8–13].

Instead, considering intra-admission outcomes, we found that laparoscopic cholecystectomy is associated with a faster recovery, shorter hospitalization, lower mortality rate, less postoperative pain and a better pulmonary function [13–26]. All these outcomes linked to the post-admission period, reflect the quality of care during the admission. Particularly, the Tiffenau Index, the ratio between forced expiratory volume in 1 s (FEV₁) and forced vital capacity (FVC), help to differentiate airflow limitations from restrictive abnormalities [15, 27].

In a more recent view, the predictive value of FEV₁, FVC and their ratio about pulmonary complications was underlined. Fuso's and Chetta's reviews support the importance of clinical relevance in assessing these respiratory outcomes. In particular, they reported that patients with lower values of respiratory parameters had an increased risk of pulmonary complications with respect to patients with normal patterns and the reduction of FEV₁ was an independent predictor of pulmonary impairment after abdominal surgery [28–30].

Within a project financed by Italian Ministry of Health 'Outcome evaluation in conventional surgery and minimally invasive surgery', we examined the scientific literature on cholecystectomy. The selected articles did not show univocal results about the efficacy of laparoscopic surgery on preserving a better pulmonary function with respect to open surgery. For this reason, we decided to synthesize the results from the scientific literature of postoperative pulmonary function. Therefore, a quantitative synthesis allows making clear which technique better preserves pulmonary function. A meta-analysis of the literature was carried out, concerning the postoperative pulmonary function in both surgical techniques, focused on the Tiffenau Index.

Materials and Methods

Search Strategy

An extensive search of the scientific literature was carried out querying electronic databases to identify relevant studies: Cochrane Controlled Trials Register, Database of Abstracts of Reviews of Effects (DARE), Embase, and Pubmed. Literature search covered the period from 1990 to 2007 because the first laparoscopic cholecystectomies were performed in the early 1990s.

The key words used to search articles were associated to interventions, population and outcomes. The following search terms were used:

- Terms related to intervention: 'laparoscopic cholecystectomy', 'open cholecystectomy', 'minimally invasive cholecystectomy', 'conventional cholecystectomy', 'traditional cholecystectomy', 'minimal access cholecystectomy', 'open versus laparoscopic cholecystectomy'.
- Terms linked to population: 'adult patients', 'surgical patients'.
- Terms related to measured outcomes: 'Tiffenau Index', 'post-operative forced vital capacity and forced expiratory volume in one second', 'postoperative pulmonary function', 'lung function', 'respiratory function', 'respiratory function test'.

A further analysis of the grey literature (those papers that were not published in primary sources) was conducted in generic search engines consulting 'Google scholar' (<http://scholar.google.com/>) and 'Vivisimo' (www.vivisimo.com), looking for unpublished studies about laparoscopic cholecystectomy.

We integrated electronic searches by hand searching, manually checking the reference lists of relevant articles and contacting experts working in the field to identify any further studies [31].

Studies in English, Italian, French and German were taken into account.

Inclusion Criteria

Referring to *study design*, we included exclusively analytical or experimental studies; descriptive studies were excluded.

Regarding *exposure criteria*, the research focused on comparison between open versus laparoscopic cholecystectomy; we excluded all articles which analyzed different surgical interventions or procedures. Studies which treated acute cholecystectomy and mini-laparoscopic cholecystectomy were also excluded.

Referring to *outcome measure*, we included in the review studies evaluating postoperative pulmonary function in terms of FVC and FEV₁ or the Tiffenau Index.

Studies that focused on different outcomes or those whose FEV₁ and FVC values were evaluated in percentages were excluded.

Only adult patients (age ≥ 18 years) were considered in the selection of the studies. We excluded studies enrolling young patients or children (age < 18 years).

Quality Assessment

The methodology of each study was assessed independently by 2 authors (L.P. and A.S.) according to a score based on a 10-point scale, consisting of 5 potential sources of bias [32, 33].

Disagreements were resolved with a third epidemiologist (G.D.) or by consensus.

Table 1. Characteristics of studies included in the meta-analysis

Authors [ref.]	Country	Year	Study design	Open	Laparo- scopic	Spirometry	Quality scores
Bablekos [14]	Greece	2003	cohort study	10	18	Med-graphics cardiorespiratory diagnostic systems	8/10
Hasukić [15]	Bosnia and Herzegovina	2002	randomized trial	28	30	Bodypletizmograf, Germany	9/10
Hendolin [16]	Finland	2000	randomized trial	22	25	Vitalograph England	10/10
Joris [17]	Belgium	1992	cohort study	15	15	Gould pulmonet 3	8/10
Karayannakis [18]	England	1996	randomized trial	40	42	Bodyscreen 2	10/10
Kimberley [19]	USA	1996	cohort study	3	29	Vitalo-graph Compact	7/10
Mimica [20]	Croatia	2000	cohort study	50	50	VICATEST-4 vitalograph	10/10
Peters [21]	USA	1993	cohort study	9	30	Cybermedic 2 plesthymograph	7/10
Putensen-Himmer [22]	Austria	1992	randomized trial	10	10	PFT-Horizon	7/10
Ravimohan [23]	India	2005	cohort study	15	40	Morgan Spiro flow 2000	6/10
Rovina [24]	Greece	1996	cohort study	25	26	Flowmate-Jaeger	8/10
Volpino [25]	Italy	1998	randomized trial	60	58	Vitalograph England	10/10
Williams [26]	USA	1993	cohort study	10	10	Med-graphics pulmonary diagnostic systems spirometer	6/10

We considered the method of allocation to study groups (random, 2, vs. quasi-random, 1, vs. selected concurrent controls, 0), data analysis and presentation of results (appropriate statistical analysis and clear presentation of results, 2, inappropriate statistical analysis or unclear presentation of results, 1, inappropriate statistical analysis and unclear presentation of results, 0), the presence of baseline differences between the groups that were potentially linked to study outcomes (of particular importance for observational studies; no baseline differences present or appropriate statistical adjustments made for differences, 2, vs. baseline differences present and no statistical adjustments made, 1, vs. baseline characteristics not reported, 0), the objectivity of the outcome (objective outcomes or subjective outcomes with blinded assessment, 2, vs. subjective outcomes with no blinding but clearly defined assessment criteria, 1, vs. subjective outcomes with no blinding and poorly defined, 0), and the completeness of follow-up for the appropriate unit of analysis (90%, 2, vs. 80–90%, 1, vs. 80% or not described, 0).

The cut-off value for including an article in our meta-analysis was 6/10.

Data Extraction and Data Analysis

Data were extracted using a standardized form referring to: authors, year of publication, study design, population, interventions, and outcomes related to postoperative pulmonary function (Tiffenau index, FEV₁, FVC).

Two authors (L.P. and A.S.) independently extracted data from the papers retrieved and corroborated their findings.

The kappa test was performed to evaluate agreement between the reviewers regarding the quality of the selected studies.

The statistical software Review Manager 4.2 was utilized for performing the meta-analysis [34].

The mean differences were calculated for continuous variables (FVC and FEV₁) with the 95% CI.

Since the selected studies evaluated FVC and FEV₁ using different spirometer devices (table 1), we calculated the standardized mean difference (SMD). According to the definition of the 'Cochrane Handbook for Systematic Reviews of Interventions', SMD is a summary statistic used in meta-analysis when all trials assess the same outcomes, but measure it in a variety of ways. It is necessary to standardize the results of the trials to a uniform scale, before they can be combined. It is calculated as the ratio between difference in mean outcome among groups and the standard deviation of outcomes among participants [35].

Heterogeneity among studies was tested by using a χ^2 test at the 0.05 significance level. A random-effects meta-analysis was applied.

A sensitivity analysis was carried out to assess the robustness of our study: we estimated the SMD for the Tiffenau index by excluding the most influential studies on the pooled estimate, i.e. the study with the higher weight and the study with the larger size effect.

Results

The combined searches resulted in a total of 370 potentially relevant studies identified by abstract and title. Of these identified trials, 357 were excluded because they did not fit our inclusion criteria. In particular, most of them considered different outcomes, different interventions, or Tiffenau Index was not evaluated. Others were excluded because they were descriptive studies or they calculated percentage values of FEV₁ and FVC, without providing baseline values (so it was not possible to calculate the means) or ratio between FEV₁ and FVC. The ma-

Fig. 1. Flow of studies through the stages of the review strategy.

jority presented unsatisfactory information, considering only laparoscopic values or only vital capacity values. The remaining 13 articles [14–26], whose publication period ranged from 1992 to 2005, met the selection criteria and were included in the meta-analysis (table 1). Among the selected articles, 5 were randomized trials [15, 16, 18, 22, 25] and the other 8 were nonrandomized [14, 17, 19–21, 23, 24, 26]. Thus, the final analysis considered a total of 680 patients: 297 underwent open cholecystectomy and 383 laparoscopic cholecystectomy.

The final agreement on selection of relevant articles was 100%.

Figure 1 shows a summary profile of the search.

The kappa test for quality analysis reports a substantial agreement between the two authors: $\kappa = 0.70$, 95% CI 0.48; 0.91 for method of allocation to study groups, $\kappa = 0.75$, 95% CI 0.55; 0.95 for data analysis and presentation

of results, $\kappa = 0.85$, 95% CI 0.69; 1.00 for presence of baseline differences between the groups, $\kappa = 0.65$, 95% CI 0.42; 0.88 for objectivity of the outcome and $\kappa = 0.70$, 95% CI 0.48; 0.91 for completeness of follow-up. No articles scored a quality value lower than cut-off (table 1).

The meta-analysis of 13 articles resulted in a SMD of 53% (95% CI 0.04, 1.02) for the Tiffenau Index in favor of laparoscopic cholecystectomy (fig. 2).

The χ^2 test analysis showed the presence of heterogeneity among studies (Tiffenau index $\chi^2 = 99.97$ $p = 0.03$), so a random effect analysis was performed.

The sensitivity analysis confirms the validity of our results. We repeated the analysis using a fixed-effects model and it showed no differences from the results of a random-effects model.

We then removed the most influential study, showing that the results of the meta-analysis were not conditioned by it (table 2).

Moreover, publication bias was not found by the funnel plot used to identify possible missing studies (fig. 3).

Discussion

The spread of laparoscopic cholecystectomy has changed the general surgeon's and indeed the public's view of the morbidity associated with abdominal surgery.

Respiratory insufficiency associated with the development of pulmonary function occupies first place on the scale of postoperative morbidity and mortality [25].

The evaluation of pulmonary function reflects the quality of care and the risks of infectious complications during the intra-admission period.

Considering that laparoscopy has a number of implications for patients, health care providers (health care professionals and facilities), the organization of health care, quality of care and society as a whole, it is important to provide quantitative evaluations on this topic for decision-makers.

Because of its potentially strategic influence as a tool for data synthesis in such highly active fields as technology assessment and outcomes research, meta-analysis may affect health care policy in a profound manner [36].

To our knowledge there has been no other meta-analysis comparing pulmonary function after laparoscopic and open cholecystectomy, and even if in the literature there are small studies concerning this topic, our attempt was to provide a synthetic result. Single studies included

Fig. 2. Forest plot of the Tiffenau Index for laparoscopic vs. open cholecystectomy.

Table 2. Sensitivity analysis

Random effect model	Fixed effect model	Analysis without most influential study for effect size (Kimberly 3.02 CI 95% = 1.59, 4.45)	Analysis without most influential study for weight (Mimica 8.67%)
0.53 CI 95% = 0.04, 1.02	0.29 CI 95% = 0.12, 0.45	0.25 CI 95% = 0.09, 0.41	0.29 CI 95% = 0.11, 0.47

in our meta-analysis show contrasting or nonsignificant results in terms of FVC and FEV₁ values or the Tiffenau Index and they also assess these surrogates on different scales, but our work provides a unique quantitative result in favor of laparoscopic cholecystectomy.

Our meta-analysis suggests that the laparoscopic compared with the laparotomic technique can reduce airflow limitations and avoid postoperative pulmonary restriction.

This should translate into a lower risk of respiratory complications, particularly in patients with underlying pulmonary disease [23].

This evidence underlines the effectiveness of laparoscopic cholecystectomy since it increases the knowledge on this specific topic and supplies a quantitative synthetic result, through a strict and reproducible technique. The studies under investigation were mostly nonran-

Fig. 3. Funnel plot.

domized (only 5 were randomized trials), therefore the results have to be interpreted with caution.

Another relevant result of our meta-analysis is the increase of the precision of the estimated effect measure reported in studies with a small sample size.

Although studies of different settings were included in our review, we used the quality score analysis to minimize the distortions related to this phenomenon.

Taking all these implications into account, we can affirm that laparoscopic cholecystectomy can preserve the postoperative pulmonary function better than open surgery, so our meta-analysis promotes the adoption of this technique as a safer alternative to traditional surgery.

Laparoscopic cholecystectomy is also associated with faster recovery, shorter hospitalization, lower mortality rate, less postoperative pain, faster return to normal activities and a better quality of life than open cholecystectomy [8–12].

Our results on the effectiveness of postoperative pulmonary function after laparoscopic cholecystectomy should be included in a health technology assessment evaluation in order to go beyond the singular experiences presented in the literature, such as cost-effectiveness evaluations.

The method of meta-analysis should be implemented in a context of health technology assessment evaluations for other minimally invasive procedures, as well as laparoscopic cholecystectomy, allowing synthetic results to be obtained and increasing the precision of the estimated effect measure.

We think that large surgical trials (RCTs) and further systematic reviews of individual patients' data for adequate pooling of results and for addressing heterogeneity should be carried out in order to provide better and updated evidence on this topic.

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