

Higher cost of single incision laparoscopic cholecystectomy due to longer operating time. A study of opportunity cost based on meta-analysis

F. FUERTES-GUIRÓ¹, M. GIRABENT-FARRÉS²

SUMMARY: Higher cost of single incision laparoscopic cholecystectomy due to longer operating time. A study of opportunity cost based on meta-analysis.

F. FUERTES-GUIRÓ, M. GIRABENT-FARRÉS

Background. We aimed to calculate the opportunity cost of the operating time to demonstrate that single incision laparoscopic cholecystectomy (SILC) is more expensive than classic laparoscopic cholecystectomy (CLC).

Methods. We identified studies comparing use of both techniques during the period 2008-2016, and to calculate the opportunity cost, we performed another search in the same period of time with an economic evaluation of classic laparoscopy. We performed a meta-analysis of the items selected in the first review considering the cost of surgery and surgical time, and we analyzed their differences. We subsequently

calculated the opportunity cost of these time differences based on the design of a cost/time variable using the data from the second literature review.

Results. Twenty-seven articles were selected from the first review: 26 for operating time (3.138 patients) and 3 for the cost of surgery (831 patients), and 3 articles from the second review. Both techniques have similar operating costs. Single incision laparoscopy surgery takes longer (16.90min) to perform ($p < 0.00001$) and this difference represents an opportunity cost of 755.97 € (cost/time unit factor of 44.73 €/min).

Conclusions. SILC costs the same as CLC, but the surgery takes longer to perform, and this difference involves an opportunity cost that increases the total cost of SILC. The value of the opportunity cost of the operating time can vary the total cost of a surgical technique and it should be included in the economic evaluation to support the decision to adopt a new surgical technique.

KEY WORDS: Opportunity cost - Single incision laparoscopic cholecystectomy - Conventional laparoscopic cholecystectomy - Economic evaluation.

Introduction

In recent years, economic arguments have become part of the healthcare field, because their premises are entirely applicable to what is happening today in our healthcare systems (1) for two reasons: first, resources are scarce; second, when resources are scarce, it is necessary to decide on the best way of spending; consequently, when resources are used in one way, they cannot be used in another.

In surgery, the use of resources always involves a sacrifice. For economists, the concept of cost always

implies renunciation. The 'opportunity cost' of surgery is defined as the value of the best option that is given up when a choice is made (2). Put another way, it is what could be done and is not done, because less appropriate options are applied (3). However, opportunity costs can rarely be found in economic evaluation studies of new technologies (4, 5).

Conventional laparoscopic cholecystectomy (CLC) is the treatment of choice for cholelithiasis. Operating times have gradually been reduced until they are shorter than in open surgery in most cases, and as such CLC is performed in most hospitals in solitary short-stay surgery or outpatient. A new technology has been developed virtually simultaneously, which is surgery via a single umbilical incision. This technique has received different names: endoscopic transumbilical surgery (TUES), embryological - NOTES (E-NOTES) and single-incision la-

¹ Department of Surgery, Universitat Internacional de Catalunya, Barcelona, Spain

² Department of Statistics, Universitat Internacional de Catalunya, Barcelona, Spain

Corresponding author: Fernando Fuertes-Guiró, e-mail: fernandofuer@gmail.com

paroscopic cholecystectomy (SILC) (6, 7), with the latter term probably describing it best. Its advantages are a lower level of surgical aggression, with faster recovery and better cosmetic results compared to the traditional laparoscopic technique, which makes it a particularly interesting approach.

Although these two techniques are routinely used in hospitals, studies have been published in recent years that compare the two technologies based on their results and their economic impact, including at meta-analysis level (8-10). However, these economic evaluation studies have conflicting results and do not analyze the opportunity cost of one technique compared to the other.

When assessing the cost of a new technology, and its opportunity cost and related variables (such as operating times), the direct healthcare costs related to the operation should be considered (the value of all goods, resources, services, hospitalization, equipment and personnel) and the costs of the side-effects of its application (in this case the aesthetic results, for example), as well as the non-health costs incurred by the patient as a result of treatment (either financial in the form of transport, people accompanying the patient, or otherwise, such as in quality of life); the productivity and costs arising from the impact on their working lives and the consequent morbimortality related to the patient receiving treatment. Taken together, these costs provide the overall cost of implementing a new technology in an economic evaluation process.

This study aims to demonstrate the importance of the opportunity cost of operating time as a cost to consider in the evaluation of new laparoscopic surgical technologies, namely laparoscopic cholecystectomy with a single incision surgery. The overall objective is a comprehensive review of the literature to determine the total cost and differences in operating times for patients between conventional laparoscopic cholecystectomy (CLC) and single incision laparoscopic cholecystectomy (SILC). Its specific objectives are as follows:

1. To identify the procedures performed by both techniques and obtain the following variables: data on surgical times and the total costs of both procedures.
2. To apply a systematic statistical approach (meta-analysis) to calculate the differences between the two technologies in the two variables above.
3. To calculate the opportunity cost of operating time of SILC.

Methods

Selected publications

For the meta-analysis, the articles were searched in the following electronic databases: Isi web of knowledge MEDLINE, EMBASE, The Cochrane Library and Scopus. Only RCT articles and controlled clinical trials in English during the period 2008-2016 were identified, using the following search terms: “traditional laparoscopic cholecystectomy”, “standard laparoscopic cholecystectomy”, “traditional laparoscopic cholecystectomy”, “three ports laparoscopic cholecystectomy”, “four ports laparoscopic cholecystectomy”, “single incision laparoscopic cholecystectomy”, “laparoendoscopic single site cholecystectomy”, “transumbilical single incision laparoendoscopic cholecystectomy”, “single port laparoendoscopic cholecystectomy”, “time”, “cost” and “economic evaluation”. The selection process was as follows:

1. All the titles and abstracts were identified by two reviewers, and disagreements resolved by consensus.
2. Once all abstracts had been identified by consensus, the two authors chose those meeting the following inclusion criteria: a) economic evaluation studies and cost analysis, cost-minimization analysis, cost-effectiveness, cost-utility analysis, cost-benefit analysis; b) interventions performed on adult patients over 18 years old; c) comparative studies of conventional laparoscopic cholecystectomy and single incision laparoscopic cholecystectomy; d) variables studied (minimum): operating time, cost of surgery, hospital stay; e) when the same author had published more than one paper, the most recent one with the highest quality was selected. The relevant articles from the abstracts selected were obtained, and those that were Congress communications, reviews, letters, editorials and case reports were discarded.
3. The exclusion criteria were comparative and non-RCT trials; studies repeated in different journals; patients undergoing other surgery associated with cholecystectomy which was performed synchronously.
4. The two reviewers analyzed the quality of the publications selected using the Evers Consensus Criteria in Health Economics (CHEC list) (11), and subsequently obtained the data necessary for the meta-analysis for each item.
5. The critical appraisal tools of CEMB (Center for

evidence-based medicine) of the University of Oxford (12) were used for evaluation the articles included in the meta-analysis study.

In addition to the above, a further strategic electronic search of the Isi web of knowledge, Medline, Embase, the Cochrane Library and Scopus was performed to calculate the opportunity cost of differences in length of the two techniques, using the search terms “laparoscopic traditional cholecystectomy” “standard laparoscopic cholecystectomy”, “traditional laparoscopic cholecystectomy”, “three ports laparoscopic cholecystectomy”, “four ports laparoscopic cholecystectomy”, “cost” and “economic evaluation,” in order to select papers meeting the following criteria: a) articles published from centers anywhere in the world in the period 2008-2016; b) economic evaluation studies of conventional laparoscopic cholecystectomy alone: economic evaluation studies and cost analysis, cost-minimization analysis, cost-effectiveness, cost-utility analysis, cost-benefit analysis; c) interventions performed on adult patients over 18 years old; d) variables studied (minimum): operating time and cost of the intervention; e) identification of articles by two reviewers and quality analysis of the publications selected by the Evers CHEC list.

Statistical study

Systematic statistical approach (meta-analysis)

The meta-analytical study, which followed the instructions of the PRISMA statment (13), considered a response variable for each item included in the study comparing CLC with SILC. The aim was to measure the magnitude of the effect, the total cost of the intervention (€) or equivalent in another currency in the year of publication and the operating time (min) according to the following definitions:

1. Total cost of the intervention: direct healthcare costs (fixed and variable) generated in the operating room by performing the surgery, and specifically: personnel costs for the duration of the operation and material costs (disposable and reusable instruments and appliances, sterilization, medication) and operating theatre use expenses.
2. Surgical time: the total time of intervention between the first skin incision and the closure of the last cutaneous wound by suture.

In the meta-analysis of both the cost and time, we have included the studies for which it was possible to extract the mean, standard deviation and sam-

ple size of each group (CLC vs SILC). The standardized mean difference (SMD) was considered as a measure of the effect size for the cost. A 95% confidence interval (CI) for the effect size is estimated in both variables. First we performed a statistical heterogeneity analysis on the studies using the Higgins and Thomson statistical test (I^2), and the χ^2 test, with $p < 0.005$ indicating statistically significant. We performed a meta-analysis and the Z test to analyze statistical significance. We conducted a sensitivity analysis (graphic influences) of the results and publication bias (Begg and Egger tests and Funnel Plot graph).

All statistical analyzes were conducted using Epidat 4.1 and Review Manager Software 5.3, developed by the Cochrane Collaboration.

Opportunity cost of operating time calculation

After estimation by meta-analysis of the difference in operating times between the two techniques, we calculated the opportunity cost of operating time represented by these differences in the time of interventions. We assumed that a surgeon should be able to perform additional surgery in the surplus time arising from using alternative surgical techniques.

This requires an actual value for the time saved when applying the most efficient surgical technique, which in our case is a cost/time (€/min) unitary factor which we will call ξ . To calculate this factor, we used data from the studies of the first literature review, as well as those in the second review using the methodology presented above. Based on these studies, we extracted the data for intervention times and costs for the period between 2008 (the start of implementation of SILC) and 2015. The value of the unit/time factor ξ is therefore calculated by dividing the average cost of the intervention in € by the average duration of surgery in minutes. This result gives the opportunity cost of operating time of the SILC, based on the value of ξ multiplied by the excess average time taken in this procedure (estimated value in the time variable meta-analysis).

Results

Literature search and selection articles

135 articles following the established protocol were obtained in the first search for the period under review. After reviewing the titles and abstracts, 79 were discarded. Copies of the full articles of the re-

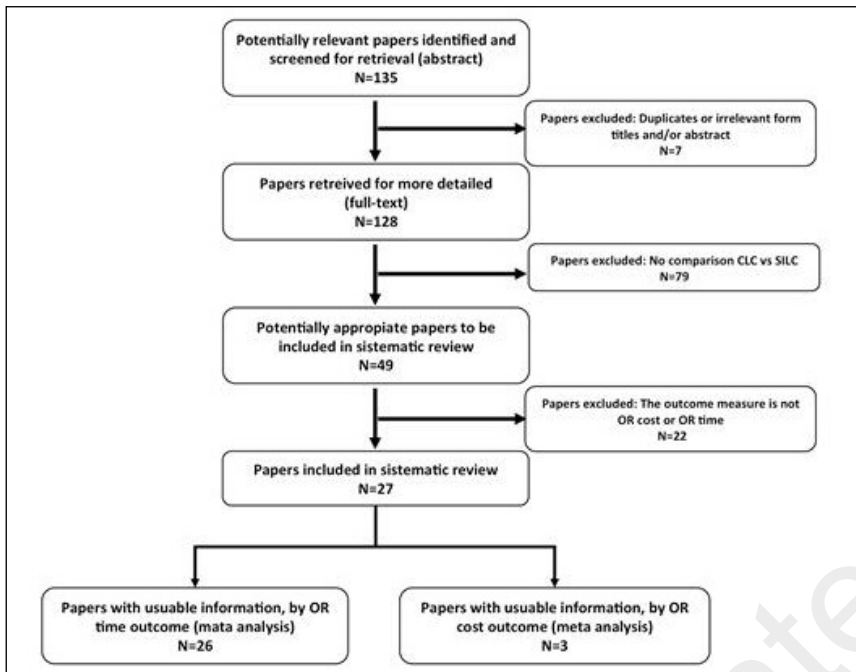


Figure 1 - Flow chart of the selection process of articles for inclusion in the meta-analysis.

maining 49 were obtained, and after reading by the reviewers and application of the Evans CHEC list, 27 articles (14-40) were finally included in this study. None of the selected items carried out a full economic assessment, but three of them contained an analysis of the costs of operations (included in the meta-analysis) and 26 papers contained surgical times (included in the meta-analysis). They all analyze laparoscopic cholecystectomy with SILC and CLC procedures (Figure 1).

The second literature search obtained 395 articles for the period under review, 184 of which were discarded (duplicates, and after reviewing the title). Another 117 were discarded after reading of the abstracts. Of the remaining 94, only 3 studies (14, 41, 42) finally included the operating costs of the procedures. The 91 discarded articles included only total hospital costs without discriminating between the different types of costs created by the patient, and as such it was impossible to obtain the operating costs in isolation (Figure 2).

In order to avoid potential risks of bias, articles published twice, those with a lack of data, those with a greater probability of failing to publish negative results, and papers not written in English were eliminated during the selection of the works for inclusion in the study.

Statistical study

After meta-analysis of the studies, the following results were obtained for each response variable.

Cost of surgery

The χ^2 test for heterogeneity was statistically significant at $p < 0.001$ and the Higgins-Thomson I^2 statistic indicates a proportion of variation between studies of 94.67%. As a result, in Figure 3 the funnel plot shows the dispersion across studies, with the Ming-Xin study being the furthest from the limits of the confidence bands.

Because of the clear heterogeneity between the studies, the pooled effects were calculated using a random-effects model reported in accordance with the Der Simonian and Laird method, which considers both within-study and between-study differences. The test for the effect indicates a $Z = 1.78$ ($p = 0.07$), indicating no statistically significant differences in cost between the two techniques of CLC and SILC. The results are shown in the forest plot in Figure 4.

The results of the sensitivity analysis are presented in Table 1, and show that the major influence on the results by the studies by Cheng et al and Pan MX et al. However, the outcome would remain the same if the former was not included, with no differ-

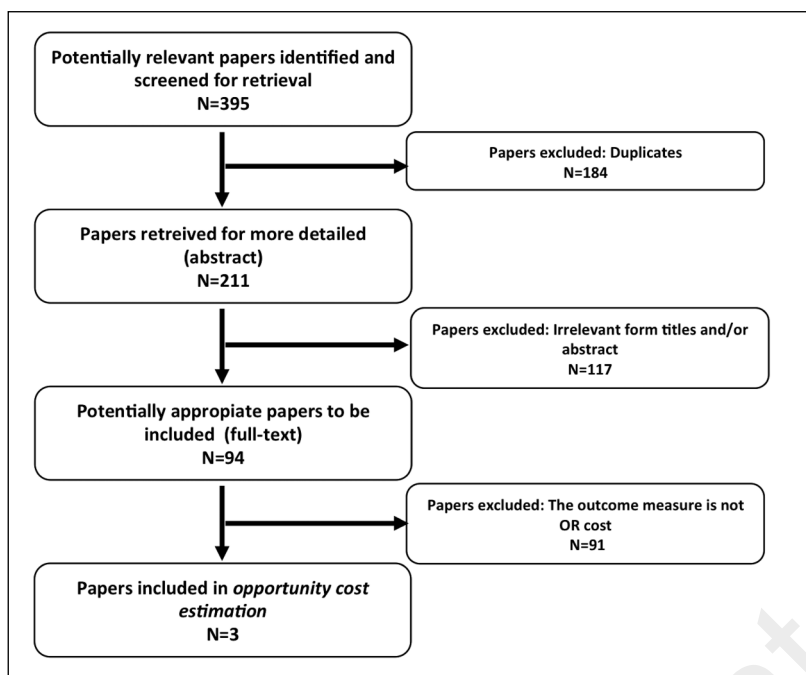


Figure 2 - Flow chart of the selection of articles for inclusion in the opportunity cost estimation.

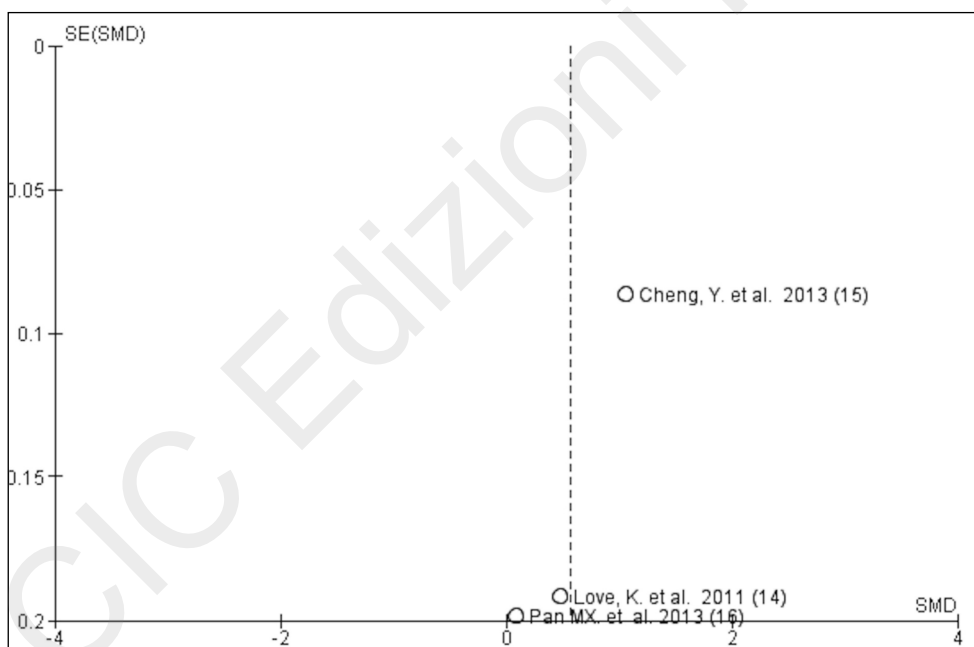


Figure 3 - Funnel plot of cost of surgery (€).

ences in cost between the two techniques, and if the latter was excluded it would be statistically significant, with the results shifting in favor of the CLC technique, i.e. the most costly. In conclusion, the studies do not have the same influence, but as the paper which could lead to a different result– Pan

MX et al - has a smaller sample size than the others and therefore has less weight in the study, the overall result including the three papers is assumed to be accurate.

Finally, in the publication bias analysis, it appears that in both Begg's test, which obtains $Z =$

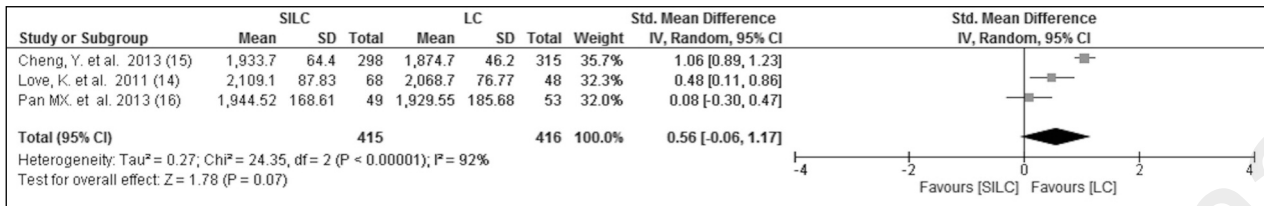


Figure 4 - Forest plot of cost of surgery (€).

TABLE 1 - SENSITIVITY ANALYSIS OF THE COST OF SURGERY (€).

Studies Included	Year	n	d	95%CI	Relative Change %
Love, K. et al. (14)	2011	116	0.5872	[-0.3660, 1.5404]	4.71
Cheng, Y. et al. (15)	2013	613	0.2876	[-0.1042, 0.6795]	-48.71
Pan MX. et al. (16)	2013	102	0.7962	[0.2365, 1.3558]	41.96
Global		831	0.5608	[-0.0543, 1.1760]	

d = mean difference between conventional laparoscopic cholecystectomy cost and single incision laparoscopic cholecystectomy cost

1.0445 ($p = 0.2963 > 0.05$) and in Egger's test, where we obtained $t = -3.7580$ ($p = 0.1656 > 0.05$), there is no apparent publication bias.

Operating time

The χ^2 test to assess heterogeneity was statistically significant at $p < 0.001$ and the Higgins-Thomson I² statistic indicates a proportion of variation between studies of 93.68%. The Funnel plot graph shows that the studies by Sharma and Chen are outside the confidence bands (Figure 5). The lack of

homogeneity between the studies led us to use a random-effects model in accordance with the Der Simonian and Laird method, and the pooled effects were calculated.

The test for the effect indicates $Z = 7.07$ ($p < 0.00001$), showing a longer time when SILC is used. The Forest Plot (Figure 6) clearly shows that the operation time differs depending on the study. However, the meta-analysis shows that there are statistically significant and relevant differences in the time spent when using the SILC (significantly longer).

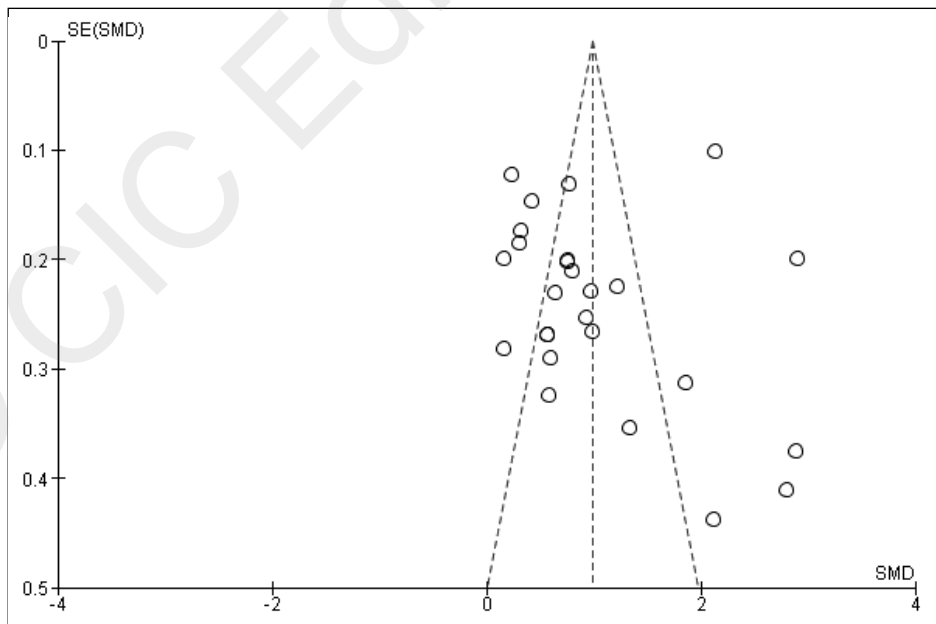


Figure 5 - Funnel plot of operating time (min).

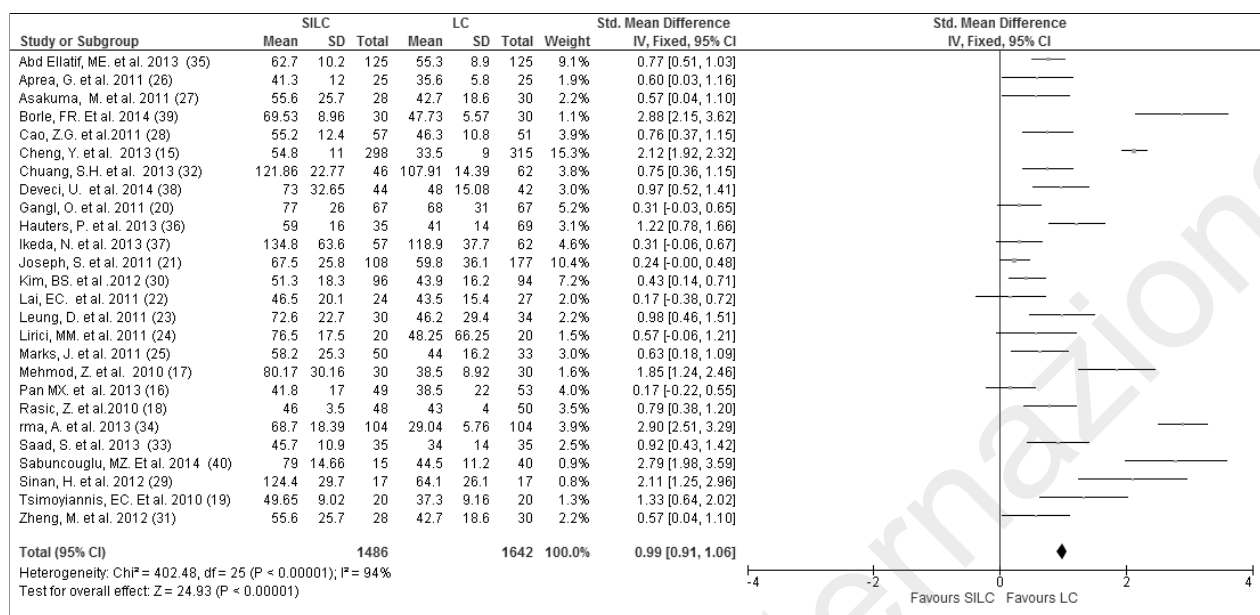


Figure 6 - Forest plot of operating time (min).

The sensitivity analysis (Table 2) shows that the results are robust, and if none of the individual studies are excluded from the meta-analysis the effect has the same direction, similar magnitude and statistical significance. No study is particularly influential, as they all make a similar contribution. The average time difference between the two techniques was estimated at 16.90 minutes (result obtained from the meta-analysis with no standardized mean difference) in a total of 3,138 patients included in the meta-analysis.

Finally, in the publication bias analysis, no apparent publication bias appears in either Begg's test ($p=0.0813>0.05$) or in Egger's test ($p = 0.7579 > 0.05$).

Opportunity cost of operating time estimation

To calculate the opportunity cost of operating time, we first obtained the average operating time for all studies of both CLC and SILC. We found that the average time was 16,90 (SD=14,51) minutes longer when SILC was used. Furthermore, a comparison of whether the time difference is statistically significant with the Wilcoxon test ($p < .00001$), indicating that the average time taken to perform surgery with the SILC is statistically longer than CLC. The average cost of the CLC according to the studies included was € 2,263.30. The value of the unit cost/time factor ξ was consequently 44.73, which means that there is an opportunity cost of using the SILC versus the CLC of € 755.97 (Table 3).

Discussion and conclusion

This study aimed to use the meta-analysis to demonstrate that the opportunity cost of operating time is a value that should be included in studies of economic costs of new surgical technologies. This new cost provides information on the economic value that is lost when a technological option is selected instead of the most cost-effective alternative. This paper also shows that this opportunity cost is crucial, as there were no significant differences in literature in the total health cost of the two techniques available (CLC and SILC).

Three articles were selected for the meta-analysis of total operating costs (the minimum required amount for meta-analysis) and 26 for the operating time, giving a total of 27. Publication bias and sensitivity was assessed with the data provided by the selected works an analysis of heterogeneity. The results of these analyses enabled us to achieve the goals outlined in the paper.

Statistical analysis of the differences between the two selected variables for both techniques shows interesting results. No differences in total operating cost between the two techniques were observed, consistent with other systematic reviews published (8-10). The three studies included in the cost analysis only dealt with the cost of the operating room, as this cost was needed to further realize the opportunity cost analysis of operating time.

TABLE 2 - SENSITIVITY ANALYSIS OF THE OPERATING TIME (min).

Studies Included	Year	n	d	95%CI	Relative Change %
Mehmod, Z. et al. (17)	2010	3068	0.9213	[0.6052, 1.2373]	-3.65
Rasic, Z. et al. (18)	2010	3030	0.9633	[0.6403, 1.2863]	0.75
Tsimoyiannis, EC. et al. (19)	2010	3088	0.9416	[0.6233, 1.26]	-1.51
Aprea, G. et al. (26)	2011	3078	0.97	[0.6504, 1.2896]	1.45
Asakuma, M. et al. (27)	2011	3070	0.9713	[0.6514, 1.2913]	1.59
Cao, Z.G. et al. (28)	2011	3020	0.9648	[0.6413, 1.2883]	0.91
Gangl, O. et al. (20)	2011	2994	0.9834	[0.6633, 1.3035]	2.86
Joseph, S. et al. (21)	2011	2843	0.9873	[0.6695, 1.305]	3.26
Lai, EC. et al. (22)	2011	3077	0.9868	[0.6696, 1.304]	3.21
Leung, D. et al. (23)	2011	3064	0.9549	[0.6341, 1.2758]	-0.12
Lirici, MM. et al. (24)	2011	3088	0.9702	[0.6513, 1.2891]	1.47
Marks, J. et al. (25)	2011	3045	0.9694	[0.6479, 1.2909]	1.39
Kim, BS. et al. (30)	2012	2938	0.9793	[0.6557, 1.3029]	2.43
Sinan, H. et al. (29)	2012	3094	0.9159	[0.6014, 1.2305]	-4.2
Zheng, M. et al. (31)	2012	3070	0.9713	[0.6514, 1.2913]	1.59
Abd Ellatif, ME. et al. (35)	2013	2878	0.9654	[0.634, 1.2968]	0.97
Cheng, Y. et al. (15)	2013	2515	0.8957	[0.6321, 1.1593]	-6.32
Chuang, S.H. et al. (32)	2013	3020	0.965	[0.6416, 1.2884]	0.93
Hauters, P. et al. (36)	2013	3024	0.9457	[0.6238, 1.2676]	-1.09
Ikeda, N. et al. (37)	2013	3009	0.9835	[0.6638, 1.3033]	2.87
Pan, MX. et al. (16).	2013	3026	0.9888	[0.6716, 1.3061]	3.42
Saad, S. et al. (33)	2013	3058	0.9575	[0.6362, 1.2789]	0.15
Sharma, A. et al. (34)	2013	2920	0.8695	[0.5898, 1.1492]	-9.06
Deveci, U. et al. (38)	2013	3042	0.9707	[0.649, 1.2923]	1.52
Borle, FR. Et al. (39)	2014	3068	0.9692	[0.6489, 1.2895]	1.37
Sabuncoglu, MZ. Et al. (40)	2014	3073	0.8911	[0.5819, 1.2002]	-6.8
Global		3128	0,9561	[0.6453, 1.2669]	

d= mean difference between conventional laparoscopic cholecystectomy cost and single incision laparoscopic cholecystectomy cost

TABLE 3 - OPPORTUNITY COST OF OPERATING TIME OF SINGLE INCISION LAPAROSCOPIC CHOLECYSTECTOMY.

Studies included	Years data included	Mean cost	CLC OR Mean cost (€)
Morris, S. et al. 2014 (41)	2011-12	2416.00	2416.00
Johner A, et al. 2013 (42)	2009	4319.87	2751.50
Love, KM. et al. 2011 (14)	2009-2010	2109.10	1622.38
Mean OR CLC cost (€)			2263.30
Mean time CLC (included in meta-analysis) (min)			50.60
Effect size of time (estimated in meta-analysis) (min)			16.90
			€
Opportunity cost of operating time estimation (€)			755.97

In the analysis of operating time, SILC appears to take longer than the CLC in cholecystectomy, i.e. an average of 16.90 minutes, in a total of 3128 patients. This difference is significant. In the other meta-analysis, where the results were mixed (8-10), some of them did not meet standards when selecting studies and including the data, making the results doubtful. This time difference may not be due to the learning curve of SILC, as some studies consider that this curve is only 10 interventions for experienced surgeons (43, 44), and as such the application of the technique itself could be associated with longer operating times.

If the economic evaluation of two surgical techniques ended here, one might conclude that the SILC costs the same as the CLC, despite the intervention lasting a little longer. However, this extra operating time has an economic value and is an opportunity cost. This additional cost changes the economic analysis of both technologies, and is the one shown in this study.

Opportunity cost estimation assigns a price to the resources used. For the operating time, we have no observable market prices and therefore in our case we calculated the unit factor cost/time ξ from the average operating cost of the CLC. We selected works from 2008, the year in which the application of the SILC began, for a value of ξ as possible date. Papers that do not make the operating cost clear, which is the only factor that matters in this study, were discarded.

In analyses of healthcare costs, the time spent by professionals in hospitals is recorded as direct expenditure (45). Consequently, this additional cost of operating time when using the SILC must be added to the total direct cost of the intervention. Our results indicate that the difference in the operating time between the two techniques is quantified at 16.90 minutes and the opportunity cost of operating time value of SILC is 755.97 €. These data show that the added cost of operating time for SILC makes this technique more expensive for the hospital. The reduced operation time when the most time-efficient technology (CLC) is used therefore allows the surgeon to be more productive.

The proposed method to calculate the opportunity cost has some limitations:

1. The model is based on the combination of data from various sources and, consequently contains differences in private practice between hospitals. This study did not address these factors, and the

findings can therefore only be applied to the centers analyzed;

2. we have assumed that the opportunity cost is based on the time it is not properly used when a less efficient technology is applied, and therefore all minutes spent in the operating room are always productive;
3. consequently, when a health center wants to determine the opportunity cost of operating time of a new technology, it must obtain information from its own operating rooms.

There is a strong international trend to adopt the criterion of efficiency as a priority factor in health (46). The analysis of the opportunity costs should be included in the economic analysis since professionals are increasingly faced with the choice between effectiveness and efficiency. The surgeon must consider its responsibility for the efficient allocation of resources and at least take into account the opportunity cost of each of these decisions implied. Ultimately streamline health expenditure, being more productive and working for the common good of society.

The search for criteria to help prioritize transparent, efficient and equitable public funding decisions for new surgical technologies should use the evidence on the relationship between the marginal benefit and marginal cost of full treatment. This would lead to innovations being rewarded based on their relative therapeutic benefit relative to the available alternatives. In national public health systems (Beveridge), a parity of therapeutic results and cost material and a waiting list for surgery, the opportunity cost of the operating time of more investments in the SILC may determine its priority in this type of surgery. In healthcare systems governed by the Bismarckian model, the weight involved in the cost of surgical time is relative because there is no social redistribution of Beveridgian models required. The prioritization is different in private health systems, as the overall aesthetic result is prioritized instead of the overall costs because the patient is paying and there is a free market.

The ability to minimize the trauma of surgery has also been established in the field of laparoscopic surgery. Efforts have been made in recent years to minimize the number and size of the trocars, up to the single access endoscopic surgery. Compared to CLC, this technique is believed to be less aggressive, with faster recovery and better cosmetic results, although there is no unanimous opinion in this regard (22, 47). Other studies suggest more safety in the

process, better control of postoperative pain and satisfaction (20, 25, 48). The main argument against this technique includes the lack of ergonomics, loss of instrumental triangulation and herniation (49). However, studies economically quantifying these advantages and disadvantages which could generate a new opportunity cost analysis have yet to be carried out.

In conclusion, single incision laparoscopic cholecystectomy costs the same as the traditional procedure, but the intervention may take longer to perform and this difference involves an opportunity cost. Financially, this additional cost significantly increases the total cost of single-incision cholecystectomy. The opportunity cost of operating time is a value that must be included in an analysis of economic costs when evaluating a new surgical technology.

Conflict of interests

Fernando Fuertes-Guiró declares that he has no conflict of interest.

Montserrat Girabent-Farrés declares that she has no conflict of interest.

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