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Systematic review

A systematic review and meta-analysis on the treatment of liver hydatid cyst: Comparing laparoscopic and open surgeries

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ABSTRACT

Background and study aims: There is an academic debate regarding surgical interventions for liver hydatid cyst disease. The purpose of the current systematic review and meta-analysis study was to analyse the pros and cons of open surgery and laparoscopic techniques, considering the outcomes of liver hydatid cysts.

Methods: Descriptive Boolean queries were used to search PubMed and Scopus for articles published between January 2000 and December 2016 to evaluate the outcomes of liver hydatid cyst in terms of mortality, post-operative complications, cure rate and recurrences. The data related to the four outcomes of liver hydatid cyst were extracted, assessed and then used as their corresponding effect sizes in the meta-analysis process.

Results: Six studies totally consisting of 1028 patients [open surgery group = 816 (+7 converted to lap) and laparoscopic group = 212] were analysed. In this meta-analysis study, random effects models of outcomes (i.e. post-operative complications, mortalities, recurrences and cure rate) of the two procedures were OR = 0.852, LL = 0.469, UL = 1.546, Z = −0.526, $p = 0.599$ (for post-operative complications); OR = 0.849, LL = 0.141, UL = 5.105, Z = −0.179, $p = 0.858$ (for mortality); OR = 0.903, LL = 0.166, UL = 4.906, Z = −0.119, $p = 0.906$ (for recurrence); and OR = 0.459, LL = 0.129, UL = 1.637, Z = −1.201, $p = 0.230$ (for cure rate). Meta-analysis and illustrated forest plots showed that there are no superiorities between the two approaches. The results of heterogeneity tests of the above mentioned outcomes were Q = 8.083, df = 5, $p = 0.152$, $I^2 = 38.142\%$ for post-operative complications; Q = 0.127, df = 2, $p = 0.938$, $I^2 = 0\%$ for mortality; Q = 4.984, df = 2, $p = 0.083$, $I^2 = 59.874\%$ for recurrence; and Q = 10.639, df = 5, $p = 0.059$, $I^2 = 53.001\%$ for cure rate.

The results of regression tests based on Egger's, smoothed variance based on Egger (SVE) and smoothed variance based on Thomson (SVT) showed that the *p values* are not significant, and there are neither significant statistical differences nor publication bias between the outcomes of the two treatment procedures.

Conclusion: The results show no promising trends towards advantages of open versus laparoscopic surgeries in the treatment of liver hydatid cyst. However, informative measurement values for comparing these surgeries could be derived for complications, recurrence, mortality and cure rates. Furthermore, all three tests, namely Egger's, SVE and SVT regression models, were used to assess publication bias and showed no evidence for the existence of publication bias.

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Introduction

Worldwide, *Echinococcus granulosus*, which was first documented in Alaska and is known as the hydatid worm, causes a parasitic infection that leads to hydatid disease. In this disease, the adult tapeworm ranging from 3 to 6 mm in length parasitises the intestine of carnivores, from which humans can unexpectedly become an intermediate host. In this disease, the tapeworms lay eggs and pass through faeces, so the digestive tract can be infected and get lysed. Each egg contains six larvae that are released into the small intestine. Then they travel through the portal system or thoracic duct to reach the liver, lung and distant organs [1,2]. For humans, 70% of the liver and 30% of the lungs can regularly be affected [2,3]. As reported in some studies, open surgery (OS) should be performed for treating echinococcosis instead of medical therapy [4], however recent WHO guidelines recommended to treat uncomplicated liver hydatid cyst (i.e. <5 cm in diameter) by the PAIR (puncture–aspiration–injection–reaspiration) procedure [5]. In the literature, there are several debates on the appropriate method for treating the liver hydatid disease [6,7]. The internationally accepted traditional treatment for this disease is to completely remove the cyst by open surgery and can be optionally performed in the patients who can tolerate the surgery. The progresses in this field have gradually increased and led to minimally invasive procedures such as laparoscopy for removing the cysts [8]. Surgical operations, whether open surgery or laparoscopy, are divided into conservative and radical procedures. In the former, the preservation of liver parenchyma is essential, while the latter includes any type of resection such as pericystectomy, segmentectomy and lobectomy [7,9].

Recently, the laparoscopic approach has been commonly used for treating the hydatid cyst disease. The laparoscopic approach has been repeatedly shown to successfully remove liver hydatid cysts; however, the need for developing a series of studies is still essential [10].

Traditionally, laparoscopic evacuation of hydatid cysts is dangerous and must be carefully performed to prevent anaphylactic reactions and seeding of intraperitoneal structures, which result from the potential leakage of the cyst contents [11].

By considering all the above facts, an important question is raised, which needs an informative answer: *by using which of the treatment procedures (open surgery (OS) or laparoscopy (Lap)) for liver hydatid cyst the patient faces low risk of complications, recurrence and mortality and high cure rate*? The rationale for reviewing the literature was (i) to determine the effect of outcomes including post-operative complications, cure rate, recurrence and mortality in OS and Lap surgeries and (ii) to determine the effect of complications between the two procedures (i.e. OS and Lap surgery).

To the best of the authors' knowledge, there are no systematic reviews and meta-analysis studies comparing open and laparoscopic surgeries for hydatid disease treatment.

Therefore, a comprehensive systematic review of the literature studies and a meta-analysis on all reported English language articles including both open surgery and laparoscopic treatment procedures for liver hydatid cysts are performed. Moreover, further, assessment and comparison of the pros and cons of the two above mentioned approaches for treating patients with uncomplicated and complicated liver hydatid cysts are necessary. Although open surgery is commonly performed for uncomplicated and complicated liver hydatid cysts, laparoscopy is mostly used for uncomplicated liver hydatid cysts [8].

Patients and methods

Meta-analysis process and meta-mums tool

To assess and pool the extracted data, we used CMA version 2.2.064 [12] and meta-mums tool. The meta-mums tool developed by us will be discussed below in details.

The meta-mums tool, developed in Matlab R2013a, is an environment for conducting the current meta-analysis study with limited features including fixed and random meta-analysis, cumulative fixed and random meta-analysis, heterogeneity test and publication bias. The above mentioned four analyses of the meta-mums tool were performed by calculating odds and log-odds ratios that are graphically illustrated using high-resolution forest plots. Heterogeneity tests were assessed by calculating Q Cochrane and I^2 [13]. Moreover, publication bias based on three tests, namely Egger's regression test [14], smoothed variance based on Egger's test (SVE) [15] and smoothed variance based on Thompson's test (SVT) [15], were generated along with funnel plots in both fixed and random meta-analysis. Furthermore, this tool did the meta-analysis within two groups by using the term "data type" as dichotomous, which included both events and the sample size of each group [13]. These data were imported, exported and illustrated as excel files and any type of image files.

Statistical analysis

Among the studies to pool the results, random effects model was used. Forest plots were used to graphically illustrate the derived results. Two heterogeneity test methods, namely the Cochran Q test (with p *value* <0.05 regarded as significant) and I^2 index, were used [13]. After generating funnel plots and performing the required regression analyses, i.e. interception of Egger's, SVE and SVT regression tests and their p *value*s, the publication bias of the study was assessed [14]. Considering various studies for assessing publication bias, a p *value* less than 0.05 was regarded significant [14–17]. The statistical analysis on all data was performed using both meta-mums tool and CMA version 2.2.0.064 [12], while only our developed tool results were proposed in this study to show that our tool can be also of interest as an alternative means for CMA in future studies. In addition to the R codes developed for SVE and SVT models available from the authors [15], these linear regression models were the extra feature implemented in the meta-mums tool in comparison to other meta-analysis software such as CMA. In addition, this property is implemented solely in the stand-alone meta-mums tool for interested meta-analysis researchers.

Systematic review procedure

To start the systematic review and meta-analysis study, a keyword-based Boolean expression approach (i.e. a Boolean query) was used to search PubMed and Scopus databases to extract and evaluate articles published from January 2000 to December 2016. According to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [18,19] for performing systematic reviews, articles relevant to surgery (conservative and radical) and laparoscopy (conservative and radical) were reviewed and analysed. The final number of remaining articles, depending on the criteria, were achieved by four of the authors. The Boolean search query used for PubMed and Scopus is as below:

Query: (((liver OR hepatic) AND (Echinococcosis OR hydatid)) AND (laparoscopy OR surgery))

The manual web-based search process extracted both published abstracts and full articles. The systematic review process was performed by identifying relevant articles retrieved from the databases by searching the field "All Fields" for possible inclusion/exclusion in/from the study. Moreover, all types of articles (i.e. full, review, systematic review, multi-organ involvement, epidemiologic studies, case studies and meta-analyses) with unclear and inadequate data were excluded. All required data were extracted from the included articles, and finally, extracted data from the

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