Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.JournalofSurgicalResearch.com

The effect of appendectomy in future tubal infertility and ectopic pregnancy: a systematic review and meta-analysis

Tarig Elraiyah, MBBS,[a,b] *Yassar Hashim, MBBS,*[c] *Mohamed Elamin, MD,*[d] *Patricia J. Erwin, MLS,*[e] *and Abdalla E. Zarroug, MD, FACS, FAAP*[f,*]

[a] *Knowledge and Evaluation Research Unit, Mayo Clinic, Rochester, Minnesota*
[b] *Center For the Science of Health Care Delivery, Mayo Clinic, Rochester, Minnesota*
[c] *Department of Surgery, Washington University School of Medicine, St Louis, Missouri*
[d] *Department of Medicine, Texas Tech University Health Science Center at Amarillo, Amarillo, Texas*
[e] *Mayo Clinic Libraries, Rochester, Minnesota*
[f] *Division of Pediatric Surgery, Mayo Clinic, Rochester, Minnesota*

ARTICLE INFO

Article history:
Received 9 July 2013
Received in revised form
16 October 2013
Accepted 18 October 2013
Available online 13 August 2014

Keywords:
Appendicitis
Appendectomy
Infertility
Ectopic pregnancy

ABSTRACT

Background: Ruptured appendicitis has been implicated in causing scarring, which can lead to infertility and/or ectopic pregnancy. To assess the degree of association and the quality of evidence supporting the relation among appendectomy, female fertility outcomes, and ectopic pregnancy.

Methods: We systematically searched multiple electronic databases from inception through May 2013 for randomized trials and observational studies. Reviewers working independently and in duplicate extracted the study characteristics, the quality of the included studies, and the outcomes of interest. Random effects meta-analysis was used to pool the odds ratio (OR) from the included studies.

Results: Our meta-analysis based on seven observational studies provided evidence that previous appendectomy is not associated with increased incidence of infertility in women (OR = 1.03, 0.86–1.24, $P = 0.71$). This finding was further augmented by several non-comparative cohorts that discussed the same issue and reported nearly the same conclusion; however, these studies pointed toward putative negative impact of surgery for complicated appendicitis on fertility. Our second meta-analysis revealed the effect of appendectomy on ectopic pregnancy was found to be significant based on a pooled estimate from four studies (OR = 1.78, 95% confidence interval = 1.46–2.16, $P < 0.0001$).

Conclusions: Appendectomy is significantly associated with an increased risk of ectopic pregnancy but not significantly associated with future infertility in women.

1. Introduction

Acute appendicitis is thought to start with obstruction of its lumen, followed by an intraluminal inflammation and distension. This leads to the ischemic necrosis of the interior wall that may eventually cause perforation if not treated [1]. It has been postulated that the perforation that complicates appendicitis can lead to intra-abdominal infection and

* *Corresponding author*. Division of Pediatric Surgery, Mayo Clinic, 200 First St. SW, Rochester, MN 55905. Tel.: +1 507 284 2623; fax: +1 507 284 0058.
E-mail address: zarroug.abdalla@mayo.edu (A.E. Zarroug).
0022-4804/$ – see front matter © 2014 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.jss.2014.08.017

scarring, which can secondarily result in obstruction of the fallopian tubes and subsequently infertility [2].

The aim of this review is to summarize the best available data assessing the magnitude of association between appendectomy, whether complicated or not, and female fertility outcomes namely infertility and ectopic pregnancy. In addition, we wanted to evaluate the body of evidence supporting that link.

2. Methods

This systematic review is protocol-driven and reported according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses statement [3].

2.1. Eligibility criteria

We included any type of study design that enrolled patients with appendicitis that underwent open or laparoscopic appendectomy and reported the outcomes of fertility and ectopic pregnancy. Studies were included regardless of size or duration of patient follow-up. We excluded articles that are not original such as review articles, commentaries, and letters. We also excluded non-English studies.

2.2. Study identification

The search strategy was designed and conducted by an experienced reference librarian (P.J.E.) with input from the study's principal investigator (A.E.Z.) and three other authors (T.E., M.E., and Y.H.). A comprehensive search of several databases from each database's earliest inclusive, dates to May 2013, was conducted. The databases included Ovid MEDLINE, Ovid EMBASE, Cochrane Library, and Scopus. We also sought recommendations from content expert for potentially relevant studies to be included in the screening process. Furthermore, we reviewed the bibliography of included articles looking for any candidate studies. The detailed search strategy is available in Appendix.

2.3. Data collection

Reviewers working independently and in duplicate screened the abstracts for eligibility. Disagreements for eligibility were automatically upgraded to the next level (full text screening). Full text of eligible abstracts were retrieved and screened in duplicate. Disagreements at this level were resolved by discussion and consensus. We calculated the inter-reviewer agreement beyond chance (kappa) during the full text screening level. Using a standardized piloted form, reviewers extracted data from all eligible studies.

For each study we abstracted the following descriptive data: description of baseline characteristics (total number of patients and age at the time of surgery), and interventions received (active or control) for all participants enrolled. We also collected the quality assessment and outcome data. A third reviewer compared the entered data and resolved inconsistencies by referring to the full-text articles.

2.4. Quality assessment

Two reviewers independently assessed the quality of studies included using the Newcastle–Ottawa scale [4]; we assessed patients' similarity to practice, adjustment for potential confounders, proportion of patients lost to follow-up, and baseline imbalances.

2.5. Statistical analysis

We pooled odds ratio (OR) and 95% confidence interval (95% CI) across included studies using random effect meta-analysis described by DerSimonian and Laird [5]. Between-studies heterogeneity was calculated by I^2 statistics, which estimates the proportion of variation in results across studies that is not due to chance [6]. Meta-analysis was completed using a comprehensive meta-analysis version 2.2 (Biostat Inc, Englewood, NJ). The quality of evidence was evaluated using the Grading of Recommendations Assessment, Development and Evaluation methods [7,8].

2.6. Subgroup analysis and publication bias:

We did not perform any subgroup analyses because of the limited amount of comparative studies that reported each outcome. Evaluation of publication bias was not feasible due to the same reason.

3. Results

3.1. Search results and included studies

The literature search yielded 350 references. Thirty abstracts met the inclusion after the initial screening, from which 19 eligible studies were selected (Fig. 1). The adjusted agreement between reviewers (kappa) averaged 0.80. We identified 19 observational studies, 9 cohorts, and 10 case-control studies; including data from 67,180 patients. Table 1 summarizes the characteristics of the included studies.

3.2. Methodological quality and risk of bias

The quality of the included studies ranges from low–moderate according to the Newcastle–Ottawa scale. The patients were

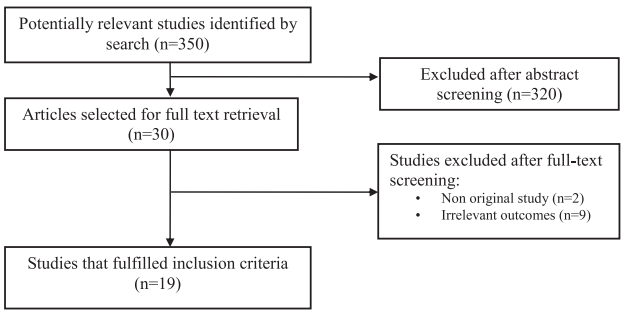

Fig. 1 – Flow diagram of how studies were screened and selected.