83398_Auto_Edited - 副本.docx

WORD COUNT	3473	TIME SUBMITTED	07-APR-2023 10:47AM
		PAPER ID	98453747

Gallbladder perforation with fistulous communication: a systematic review

GBP with fistulous communication

Alejandro Quiroga-Garza, Neri Alejandro Alvarez-Villalobos, Milton Alberto Muñoz-Lejia, Mariano Garcia-Campa, Hermilo Jeptef Angeles-Mar, Guillermo Jacobo-Baca, Rodrigo Enrique Elizondo-Omana, Santos Guzman-Lopez

Abstract

BACKGROUND

The management of gallbladder perforation (GBP) with fistulous communication (Neimeier type I) is controversial.

AIM

This systematic review aimed to recommend management options.

METHODS

A systematic review of studies describing the management of Neimeier type I GBP was performed according to PRISMA. The search strategy was conducted in SCOPUS, Web of Science, MEDLINE, and EMBASE (May 2022). Data extraction was obtained for patient characteristics, type of intervention, days of hospitalization (DoH), complications, and site of fistulous communication.

RESULTS

A total of 54 patients (61% female) from case reports, series, and cohorts were included. The most frequently fistulous communication was the abdominal wall. Patients from case reports/series had a similar proportion of complications between open cholecystectomy (OP) and laparoscopic cholecystectomy (LC) (28.6 *vs* 12.5; $P = 0.569$). Mortality was higher in OC (14.3 *vs* 0; $P = 0.467$) but this proportion was given by only one patient. DoH was higher in OC (mean 26.3 *vs* 6.6 days). There was no clear association between higher rates of complications of a given intervention in cohorts, and no mortality was observed.

CONCLUSION

Surgeons must evaluate the advantages and disadvantages of the therapeutic options. OC and LC are adequate options for the surgical management of GBP, with no significant differences.

Key Words: Gallbladder Perforation; Open cholecystectomy; Laparoscopic Cholecystectomy; fistulous communication.

Core Tip: Gallbladder perforations are rare. Management guidelines are non-specific. Although a clear benefit between open and laparoscopic cholecystectomy is lacking, with the increase in laparoscopic training and availability, this approach may demonstrate superiority in time.

INTRODUCTION

Gallbladder (GB) disease is a common pathology. Complications such as spontaneous (non-traumatic) gallbladder perforation (GBP) due to gallstone disease are rare, ranging from 0.8 to 15%, with a mortality of 12 to 16% [1-3]. It is caused by a cascade of events, starting with an obstruction causing bile stasis with bacterial proliferation, distension, increased pressure, and vascular and lymphatic collapse, which turns to ischemia, necrosis, and finally perforation [3,4]. The most common site of perforation is the fundus, as it has the lowest vascular supply [5].

Acute cholecystitis may be classified into different grades of severity using the Tokyo guidelines or the Parkland classification [6,7]. However, GBP itself can be classified into 3 types according to Neimeier. Type I for chronic perforation with fistulous communication (cholecystoenteric fistulae); type II for subacute perforation with a surrounding abscess contained by adhesions; type III for acute perforation and spillage to the cavity with generalized biliary peritonitis [8]. Due to a historically erroneous cite, authors frequently switch types I and III, a reason why it is important to specify the characteristics of the perforation [1-3,8-12].

Management protocols are well established in acute cholecystitis, but GBP remains controversial. Preoperative diagnosis is difficult, usually only identified in half the cases [13]. Abdominal computed tomography (CT) provides the most sensitive and specific imaging tool allowing the evaluation of surrounding structures [1-3,14]. A recent

systematic review of localized GBP established open cholecystectomy has a lower incidence of requiring added procedures and a lower rate of postoperative complications [13], however recent cohorts support laparoscopic management [10,12,15]. Recommendations will need to be reviewed as more current studies are added to the available literature. Fistulous communication has not been studied in detail and may vary depending on the organ/cavity of communication [16-19]. This systematic review aims to evidence the management of chronic GBP with fistulous communication regarding the type of surgical intervention, timing, and complications.

MATERIALS AND METHODS

Design and registration

This study adheres to the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) statement [20]. It was successfully registered in the International Prospective Register of Systematic Reviews (PROSPERO, NIHR) under the ID: CRD42021275733. It was also reviewed and approved by the University's Ethics and Research Committees with the registration number RV21-0019

Eligibility criteria

Studies with the following criteria were included in this review: (1) randomized controlled trials (RCTs), quasi-RCTs, and observational studies (cohorts, case studies, case series) that compare/reported open cholecystectomy (OC) and/or laparoscopic cholecystectomy (LC) for Neimeier Type I GBP in adult patients (>18 years old). The intervention must have been open or laparoscopic cholecystectomy and patients could have received another intervention either before or after the interventions of interest; (2) reported mean days of hospitalization (set as primary outcome), complications related to the surgical intervention, need of another intervention after OC/LC (the interventions did not resolve the GBP), mortality, fistulation organ, and need of intensive care unit (ICU) admission; (3) reported in English or Spanish. Exclusion criteria included: studies in which GBP Neimeier type I diagnosis was unclear. No restrictions were applied in terms of study setting or time frame.

Data Sources and Search Strategy

An experienced librarian designed and conducted the search strategy in the following databases in May 2022: Scopus, Web of Science, MEDLINE, and EMBASE. An additional search was performed on Google Scholar. The initial strategy was complemented by screening the reference lists from the selected studies to identify any potentially relevant studies that may have been missed, searching for clinical trial registries, and contacting experts in the field to identify any unpublished or in-progress eligible studies.

Data management

All search results were uploaded to EndNote X8 for de-duplication. The resulting studies were uploaded to Distiller Systematic Review (DSR) software for both title/abstract and full-text screening. All results from the search strategy were documented per database before and after de-duplication.

Study selection process

Study selection took place in two phases (title/abstract and full-text screening). Through each phase of the review, two reviewers worked independently and in duplicate to assess the eligibility of the studies. Chance-adjusted inter-rater agreement was assessed at each phase using the Kappa statistic [21]. Before each phase of screening, a pilot test with a random sample of studies from the search strategy results was carried out to standardize the reviewers' criteria. Disagreements were discussed and criteria were adapted if necessary. The pilot tests were repeated until a Kappa index of (>0.70) was reached. In the first phase, the title and abstract of all the studies obtained from the search strategy were screened and reviewers selected the eligible articles based on the inclusion criteria. During this phase, discordant decisions passed to the full-text phase to achieve a highly sensitive selection. Eligibility was then assessed through a full-text screening. Disagreements between the reviewers during this second phase were resolved by consensus and if it was not achieved, a third reviewer arbitrated the evaluation. During the entire process, the number of included and excluded articles, and the reasons for the exclusion were documented.

Data collection process

Two independent reviewers working in duplicate collected data for all eligible articles using a web-based data extraction form. The information obtained included: the type of study, author information, follow-up, year of publication, baseline characteristics of patients, type of intervention, days of hospitalization, days from diagnosis to intervention, complications, mortality, ICU admission, site of perforation, and fistulous communication. Disagreements were resolved by consensus, and if an agreement was not reached, a third reviewer had the final decision.

Missing data

If any data important for the outcomes were missing or unclear, the corresponding author was contacted *via* e-mail to clarify the situation. After a lapse of 10 days, a second email was sent to non-responders, and if there still was no response, other authors were contacted. If with all the attempts no response was received, the data or study was excluded.

Risk of bias and quality assessment

Two reviewers working independently and in duplicate evaluated the risk of bias from the studies using the Cochrane's ROBINS-I tool for the quasi-RCTs and observational studies [22], and the tool for assessing the methodological quality of case reports/series proposed by Murad *et al* for case reports/series [23]. Any disagreement during this process was resolved by consensus or, if not achieved, by a third reviewer's arbitration.

Data Synthesis

The studies included are described as a narrative synthesis in a table including study design and setting, sample size, target population characteristics, description of the intervention, study groups, type of outcomes, and the level of risk of bias.

SPSS version 25 [24], and RevMan5 [25] were used for statistical analysis. The outcomes were summarized and presented as means with standard deviation for the primary outcome. Dichotomous outcomes were presented as the number of events and proportions. Categorical variables were analyzed using the Chi-squared test, and T-student test for independent groups for continuous numerical variables. If two or more

studies were homogenous enough a cumulative meta-analysis was performed. A random-effects model was used with X^2 test and I^2 statistic to assess heterogeneity between studies. The X^2 cut-off value of $p \leq 0.10$ and an I^2 value >50% were considered indicative of considerable heterogeneity. For all statistical analyses, a p-value of <0.05 was considered statistically significant. If this was not achieved, clinical outcomes were summarized narratively.

RESULTS

Study Characteristics

There was a sustainable level of agreement between reviewers in the title & abstract screening phase (k= 0.72) and full-text phase (k=0.86). A total of 1443 studies were identified and screened, with 210 included for full-text screening. After both screening phases, 18 studies were included for the qualitative and quantitative synthesis of fifteen case reports/series and two cohort studies (Figure 1). Across all studies, no conflict of interest was observed. Most studies were published ≥2016 (n = 47 patients vs. 8 from ≤2015) with 26 of the 55 total patients managed with LC (Table 1).

Patients Characteristics

A total of 20 patients were included from case reports/series, with a mean age of 66.6 ± 17.6, of which 65% were female (Table 2). Nine patients denied comorbidities. The most common comorbidity was diabetes mellitus followed by cardiovascular diseases (Supplement Table 1). Preoperative diagnosis was identified as a cholecystic fistula in 16 patients (4 not reported). The most utilized diagnostic imaging tool was abdominal ultrasound (US) and computed tomography (CT). The most common site of GBP was the fundus (n = 5) with communication to the abdominal wall (n = 11). Eight patients were treated with LC, but 3 were converted to OC, making it the most common (n = 12) approach. Four patients were managed conservatively, while 3 required added Endoscopic Retrograde Cholangiopancreatography (ERCP). One patient with a pleural fistula required a chest tube. Patients treated conservatively had a shorter evolution time of symptoms to their admission to the emergency room (ER) with 141.5 days

(range 13-270), compared to those treated with OC (265 days, range 10-730) and LC (174.2 days, range 2-730). Patients undergoing OC had a shorter range of 7-18 days from their ER admission to the operating room (OR) compared to those undergoing LC with a range of 16-34 days. No patient was admitted to the intensive care unit (ICU). OC had longer mean days of hospitalization (DoH) than LC (26.3 *vs* 7.0, p 0.277) (Table 3).

A total of 35 patients were included from two cohort studies, with a mean age of 62.45 years, of which 60% were female (Table 4). Similar to case reports/series, the most common comorbidities were cardiovascular diseases (n = 7) and diabetes mellitus (n = 7). The most frequent site of perforation was the gallbladder´s body (n = 16) followed by the fundus (n = 14). Less than half (n = 13) were diagnosed pre-operatively. One study favored OC (n 17/20) with a higher mean of DoH (10.6 days), while the other study favored LC (n 14/15) with a shorter mean of DoH (1.69 days), although this was from a larger sample, and not only fistulous GBP.

Risk of Bias & Quality Assessment

Both cohort studies included had a moderate risk of bias. This was due to concerns in the domains of bias due to confounding, and bias in the measurement of outcomes due to the lack of blinding (Supplement Table 2). Except for 2 case reports and 1 case series which had an overall low risk of bias, the rest presented a moderate risk of bias. This was most commonly due to the patient(s) selection, as it did not represent the whole experience of the investigator's center (Supplement Table 3).

Surgical Intervention Outcomes

In patients from case reports/series (Table 3), there was a similar proportion of patients presenting any complication post-OC and post-LC (28.6 *vs* 12.5%; P = 0.569). LC had a higher proportion of need for another intervention compared to OC, although this outcome was not statistically significant. The mortality proportion was higher in OC than in LC (14.3 *vs* 0%; P = 0.467), but this was given by only one patient. DoH was higher in patients undergoing OC than LC (mean 26.3 *vs* 6.6 days), although this outcome was not statistically significant (P = 0.277). Patients receiving conservative treatment did not present any morbidity or mortality.

In patients from included cohort studies, no mortality was observed in either intervention. Two patients in the LC group and seven in the OC group presented a complication after the intervention. However, there was no clear association between higher rates of complications of a given intervention (OR 0.33, 95%CI 0.03-3.31; I^2=0%, *P* = 0.64). Three LC were converted to OC and none of the OC needed another intervention (Figure 2).

DISCUSSION

This systematic review summarized the management of patients with Niemeir Type I GBP (perforation with a fistulous tract). A fistulous communication may be formed as a result of chronic GBP with various structures. There is a higher prevalence in women, and the abdominal wall was the most common site, followed by hollow viscera (stomach, duodenum, colon), and one case of the pleural cavity [36,42-44]. There was no statistically significant difference between OC and LC, however, LC tended to have less DoH, in both case reports/series and cohorts.

The first report of this rare complication was described in 1670 by Thilesus [42]. In 1890 Courvoisier reported 169 cases of spontaneous cholecystocutaneous fistulae [45]. The most commonly reported cutaneous communication was in the right upper quadrant, however, the left upper quadrant, right iliac fossa, periumbilical, anterior chest wall, and gluteal region have been described [32,40,42,46-48]. The ideal imagining modalities for the diagnosis are ultrasonography followed by CT with a fistulography. Clinical management includes analgesic therapy, antimicrobial, and individualized surgical treatment. OC and LC are both described as ideal surgical options for scheduled interventions. Complete excision of the fistulous tract is the recommended surgical treatment. Conservative approaches such as percutaneous cholecystectomy with drain insertion may be considered for high-risk patients or in palliative care settings [13,49].

Gastric and duodenum fistulae were the most common internal communications. This is due to their anatomical proximity to the gallbladder. US and CT are helpful in diagnosis, most of these being identified preoperatively, however, 22% of hollow

visceral communications were transoperative findings [50]. OC was the preferred approach, with a conversion rate of 37.5% in LC (n = 3/8).

The cholecystocolic fistulae were also reported. These have been associated with other pathologies such as a history of gastric surgery, diverticular disease, trauma, or gallbladder carcinoma. Most of the patients are asymptomatic, however, diarrhea, right upper abdominal pain, fever, and jaundice can be present, and rarely hemorrhage, sepsis or extraperitoneal abscess [44,46]. Savvidou *et al* proposed a triad of pneumobilia, chronic diarrhea, and vitamin K malabsorption to be pathognomonic of a chlolecystocolic fistula [38]. The clinical presentation of both reported cases had watery diarrhea and weight loss in common. Cholecystectomy with resection of the fistulous tract is the standard treatment, although in difficult cases a partial colonic resection may be required [30,46].

The reported cholecystopleural fistula was diagnosed by US and CT. The patient presented with malaise, vomiting, and dyspnea. The presence of E. Coli in the thoracentesis confirmed the imaging diagnosis. A laparoscopic approach with fistulous communication resection was decided to avoid negative pressure drainage with a chest tube [17]. A thoracic *vs* abdominal approach for the resection is still controversial [26].

The predominant site of GBP for fistulous communication was equal between the fundus (n = 19) and body (n = 19). The healing of the gallbladder due to the chronicity of the pathology may influence this, as the fundus has been described as the most common site of perforation due to the lowest vascular supply [5].

A chronic GBP with fistulous communication with the bile duct may be classified as Niemeier type I, but is more commonly known as the Mirizzi syndrome. A chronic inflammation is caused by a calculus stuck in the Hartmann or neck of the gallbladder, creating a fistula with the biliary tract. Mirizzi syndrome should be considered separately and recommendations made independently, as it requires urgent surgical intervention due to the obstruction of the biliary tract, and its implications [51-53]. Niemeier type I can be scheduled when the patient's clinical state allows it, and even be managed conservatively in unstable patients.

More studies detailing the GBP characteristics and management are needed to update current guidelines. No difference was established between OC and LC, with half the cases in recent years managed conventionally. To choose the optimal surgical technique, the surgeon must evaluate the advantages and disadvantages of the therapeutic options, the resources available in their environment, and their expertise. In patients with multiple co-morbidities and a high risk of trans- and post-operative complications, conservative medical treatment should be considered.

Limitations

More cohort studies are needed to ascertain the effects estimates of the outcomes. Cohorts need to include subgroup analysis to delve across specific groups with GBP. The current cohorts do not specify the organ/structure of fistulous communication, limiting a proposal of management options based on organ/structure. Many of the corresponding authors did not respond to emails, or could not provide the specific data needed. Some strength of this systematic review and meta-analysis was the rigorous methodology performed across all the steps of the review (search strategy-data analysis).

CONCLUSION

Open and Laparoscopic cholecystectomy are adequate options for surgical management of Neimeier type I gallbladder perforation, with no significant differences in complications, DoH, or need for other interventions.

Figure Legends

Figure 1 CONSORT Diagram. GBP 1: gallbladder perforation Neiemier type 1; LC: laparoscopic cholecystectomy; OC: open cholecystectomy.

Figure 2 Post- Intervention Complications after cholecystectomy. LC: laparoscopic cholecystectomy; OC: open cholecystectomy; CI: confidence interval.

Table 1. Surgical Treatment from Case Report/Series Studies and Cohorts.

Year	Patients with Type I GBP	Men	Women	Lap Chol			Open Chol			Conservative treatment
				n	Qx pre	Qx post	n	Qx pre	Qx post	
≤2005	2	1	1	1	1	0	0	0	0	1
2006-2010	3	1	2	0	0	0	2	0	0	1
2011-2015	3	0	3	1	0	0	1	0	0	1
2016-2020	25	11	14	19	0	0	5	0	1	1
≥2021	22	5	17	5	4	0	17	4	0	0

*GBP: Gallbladder perforation; Lap Chol: Laparoscopic cholecystectomy; Open Chol: Open cholecystectomy; Qx: Surgery or procedure; pre: previous to the cholecystectomy; post: after the cholecystectomy

Table 2. Patient Characteristics of Case Reports/Series

Fistulous communication	N (fem)	Site of Perforation			Preoperative Diagnosis	Laparoscopic Cholecystectomy (converted)	Open Cholecystectomy	Conservative	Added Procedures
		Fundus	Body	Neck					
Abdominal wall	11 (8)	3	3	3	9	3 (1)	7	1	1 ERCP
Gastric	4 (4)	-	-	1	2	2	1	1	
Duodenum	3 (1)	-	-	-	3	2 (2)	2	1	1 ERCP
Colon	2 (1)	2	-	-	2	0	2	0	1 ERCP

Pleura	1 (0)	-	-	-	1	1	0	0	1 Pleural tube
Total	**20 (13)***	**5**	**3**	**3***	**16***	**8 (3)**	**12**	**3**	**4**

N: Sample size; fem: female; converted: laparoscopic cholecystectomy converted to open; ERCP: Endoscopic Retrograde Cholangiopancreatography; *: one patient had both abdominal wall and gastric fistula.

Table 3. Surgical Outcomes in Case Report/Series Patients

Surgical Approach	**n**	**Cx**	p-value	**Convertion**	p-value	**Mortality**	p-value	**DoH**	p-value
Open Chol	7	2	0.550	NA	0.213	1	0.438	26.3 (± 22.7*)	0.277
Lap Chol	9	1		3		0		7.0 (± 5.1*)	

Four patients were not included in this analysis due to their conservative management. DoH: Days of Hospitalization *: reported as mean (± standard deviation).
1
P-value was calculated using Chi-square test, with statistical significance set at <0.05

Table 4. Patient Characteristics of Cohort Studies

Author Year Country	**N (fem)**	**Mean Age**	**Site of Perforation**			**Preoperative Diagnosis**	**Laparoscopic Cholecystectomy (converted)**	**Open Cholecystectomy**	**Conservative**	**Added Procedures**	**DoH post-chol**
			Fundus	**Body**	**Neck**						

Gupta et al. 2021 India [10]	20 (16)	53.1	7	11	2	2	3 (0)	17	0	8	10.64 ± 6.39
Sahbaz et al. 2017 Turkay [42]	15 (5)	71.8	7	5	2	11	14 (0)	1	0	0	1.69*

N: Sample size; fem: female; converted: laparoscopic cholecystectomy converted to open; added procedures included 5 common bile duct explorations and 3 choledochoduodenostomies); DoH post-chol: days of hospitalization post-cholecystectomy; *: not specific to GBP type 3 (data from 133 patients with GBP).

83398_Auto_Edited - 副本.docx

ORIGINALITY REPORT

24%
SIMILARITY INDEX

PRIMARY SOURCES

1	Alejandro Quiroga-Garza, Neri Alejandro Alvarez-Villalobos, Hermilo Jeptef Angeles-Mar, Mariano Garcia-Campa et al. "Localized Gallbladder perforation: a systematic review of treatment and prognosis", HPB, 2021 Crossref	162 words	4%
2	mail.ijsurgery.com Internet	132 words	4%
3	www.ncbi.nlm.nih.gov Internet	110 words	3%
4	link.springer.com Internet	67 words	2%
5	ped-rheum.biomedcentral.com Internet	52 words	1%
6	Philipp Kasper, Julia Kaminiorz, Christoph Schramm, Tobias Goeser. "Spontaneous cholecystocutaneous fistula: an uncommon complication of acute cholecystitis", BMJ Case Reports, 2020 Crossref	36 words	1%
7	Sonia Chavez‐Alvarez, Maira Herz‐Ruelas, Ana Karina Raygoza‐Cortez, Yeudiel Suro‐Santos et al. "Oral mini‐pulse therapy in vitiligo: a systematic review", International Journal of Dermatology, 2021	35 words	1%

Crossref

8 Edgar Gerardo Dorsey-Treviño, Belinda Maricela Contreras-Garza, José Gerardo González-González, Neri Álvarez-Villalobos et al. "Systematic review and meta-analysis of the effect of SGLT-2 inhibitors on microvascular outcomes in patients with type 2 diabetes: a review protocol", BMJ Open, 2018 — 34 words — 1%
Crossref

9 Carolina Quintanilla-Sánchez, Alejandro Salcido-Montenegro, José Gerardo González-González, René Rodríguez-Gutiérrez. "Acute cerebrovascular events in severe and nonsevere COVID-19 patients: a systematic review and meta-analysis", Reviews in the Neurosciences, 2022 — 23 words — 1%
Crossref

10 www.researchgate.net — 17 words — < 1%
Internet

11 publishing.rcseng.ac.uk — 16 words — < 1%
Internet

12 www.science.gov — 16 words — < 1%
Internet

13 epos.myesr.org — 15 words — < 1%
Internet

14 Mariana Garcia-Leal, Ana Laura de Leon-Ibarra, Pablo J. Moreno-Pena, Ivan Hernandez-Galarza et al. "Silicone breast implants and connective tissue diseases: How does current evidence add to the no-association consensus? Systematic review and meta-analysis", Women & Health, 2022 — 14 words — < 1%
Crossref

15	Rene Rodriguez-Gutierrez, Andrea Flores-Rodríguez, Karina Raygoza-Cortez, Mariana Garcia-Leal et al. "Intensive vs. conventional blood pressure goals in older patients with type 2 diabetes: a systematic review and meta-analysis", Endocrine, 2022 Crossref	14 words — < 1%
16	f6publishing.blob.core.windows.net Internet	14 words — < 1%
17	www.mdpi.com Internet	12 words — < 1%
18	www.medrxiv.org Internet	12 words — < 1%
19	www.ijsurgery.com Internet	11 words — < 1%
20	Mueller, D.. "Reported effects in randomized controlled trials were compared with those of nonrandomized trials in cholecystectomy", Journal of Clinical Epidemiology, 201010 Crossref	9 words — < 1%
21	theses.gla.ac.uk Internet	9 words — < 1%
22	www.scielo.br Internet	9 words — < 1%
23	Flores Villanueva Luis Gerardo. "Evaluacion pre y postpieloplastia de indice de resistencias vasculares intrarrenales en pacientes con obstruccion ureteropelvica", TESIUNAM, 2004 Publications	8 words — < 1%

24 Jukka Karvonen, Paulina Salminen, Juha M. Grönroos. "Bile duct injuries during open and laparoscopic cholecystectomy in the laparoscopic era: alarming trends", Surgical Endoscopy, 2011
Crossref
8 words — < 1%

25 www.pubmedcentral.nih.gov
Internet
8 words — < 1%

26 Fernando García-Rodríguez, Karina Raygoza-Cortez, Lesli Moreno-Hernandez, Rodrigo García-Pérez et al. "Outcomes of transitional care programs on adolescent chronic inflammatory systemic diseases: systematic review and meta-analyses", Pediatric Rheumatology, 2022
Crossref
7 words — < 1%

27 Luis H. Sordia-Hernandez, Felipe A. Morales Martinez, Eduardo Gutierrez Orozco, Andrea Flores-Rodriguez et al. "The Effect of Post warming Culture Period Between Thawing and Transfer of Cryopreserved Embryos on Reproductive Outcomes After In Vitro Fertilization (IVF): A Systematic Review and Meta-analysis", Journal of Reproduction & Infertility, 2021
Crossref
6 words — < 1%

EXCLUDE QUOTES	OFF	EXCLUDE SOURCES	OFF
EXCLUDE BIBLIOGRAPHY	OFF	EXCLUDE MATCHES	OFF