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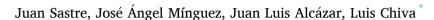
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Full length article

Microsurgical anastomosis of the fallopian tubes after tubal ligation: a systematic review and meta-analysis





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Objective: Between 20% and 30% of women who have undergone tubal ligation regret their decision. The alternative to regain fertility for these women is either in vitro fertilization or tubal re-anastomosis. This article presents a systematic review with meta-analysis to assess the current evidence on the efficacy of tubal recanalization surgery in patients who have previously undergone tubal ligation. Study design: The search was conducted in the World of Science (WOS) database, The Cochrane Library and ClinicalTrials.gov record using the keywords "tubal reversal", "tubal reanastomosis" and "tubal anastomosis". The review was carried out by two of the authors. Data from 22 studies were evaluated, comprising over 14,113 patients who underwent the studied surgery, following strict inclusion criteria: articles published betweer January 2012 and June 2022, in English and with a sample size bigger than 10 patients were included. A random-effects meta-analysis was performed. Results: The overall pregnancy rate after anastomosis was found to be 65.3 % (95 % CI: 61.0–69.6). The percentage of women who had at least one live birth, known as the birth rate, was 42.6 % (95 % CI: 34.9–51.4). Adverse outcomes after surgery were also examined: the observed abortion rate among women who underwent surgery was 9.4 % (95 % CI: 7.0–11.7), and the overall ectopic pregnancy rate was 6.8 % (95 % CI: 4.6–9.0). Not differences were found between the outcomes when differentiating surgical approaches: laparotomy, laparoscopy, or robotic-assisted surgery. The patient's age was identified as the most significant determining factor for fertility restoration. Finally, when comparing the results of tubal reversal with in vitro fertilization, reversal procedures appear more favorable for patients over 35 years old, while the results are similar for patients under 35 years old, but more data is needed to evaluate this finding.

Introduction

Tubal ligation (TL) is a surgical technique chosen by some women as a form of permanent contraception. Based on the Fertility Survey published in 2019 by the National Institute of Statistics, it is reported that in Spain there are over 600,000 women who have opted for surgical sterilization as their chosen contraceptive method [1]. Several studies show that up to 20–30 % of women who undergo TL regret having done so [2–4]. Among female contraceptive methods, TL is the most widespread definitive surgical option. This technique can be performed through open surgery or minimally invasive surgery Minimally invasive surgery is usually the most commonly used form.

Currently, when a woman who has undergone this surgery wants to

become pregnant again, there are two options in practice: undergo assisted reproduction technology or tubal anastomosis [5]. Tubal anastomosis, tubal reversal, or tubal recanalization are the different names given to the surgical process aimed at recovering fertility after TL surgery. Tubal anastomosis surgery has been performed since the late 1960s [6]. The technique has been improved over the years. It began with laparotomy and currently there are several groups in the world that perform it using minimally invasive surgical techniques: laparoscopy or robotic assistance [7].

The surgical technique generally involves removing the tied tissue from the Fallopian tube. Subsequently, end-to-end anastomosis is performed using different types of approaches [8].

The first surgical approach used was the open technique or

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Received 10 August 2023; Received in revised form 4 October 2023; Accepted 12 October 2023 Available online 23 October 2023 0301-2115/© 2023 The Author(s). Published by Elsevier B.V. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/). laparotomy over the 1960s. The laparoscopic approach did not take long to arrive and has been implemented in recent years. Over time, surgical solutions have been developed to improve the quality of anastomosis, particularly through robotic surgery. The first reported surgery in which tubal anastomosis was performed with robotic assistance was in 1998, resulting in success [9].

Much has been written and published about this surgery, but it is still sometimes unknown to patients as an option for restoring their fertility and giving them the opportunity to become mothers again. This option is often overshadowed by in vitro fertilization (IVF) techniques, which are generally a more expensive treatment and involve controversial ethical aspects for some couples [10].

This systematic review is designed to evaluate the efficacy in restoration of fertility in women undergoing anastomosis after TL.

Material and methods

Search

The search tool used was the platform Web Of Science, which contains a collection of databases such as MEDLINE, Scielo Citation Index, Korean Citation Index, Russian Science Citation Index and of course databases belonging to the Core Collection. We also looked up for publication in the record of ClinicalTrials.gov and The Cochrane Library. We searched for randomized and non-randomized studies on sterilization reversal from June 2012 up to June 2022. A search strategy was established using the keywords: "tubal reversal", "tubal reanastomosis" and "tubal anastomosis".

The review was carried out by two of the authors involved. This search was limited to English-language articles that addressed human research and had an abstract. Participants were women seeking to restore their fertility following tubal sterilization, and the sample size of the studies needed to be equal to or greater than 10 patients. Various study designs were accepted, including prospective or retrospective studies, randomized controlled trials, cohort studies, reviews, casecontrol studies, and case series. There were no age restrictions. Exclusion criteria excluded studies such as individual case reports, descriptive opinion articles without patient data, or patient studies with a sample size of less than 10 cases. Articles contained within other publications (e. g., systematic reviews) were also excluded.

Study selection

The included studies were evaluated using the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) checklist [31]. The quality of the studies was assessed in terms of participant inclusion criteria, selection bias, and the description of confounders. The overall quality of the included studies was determined based on their internal validity, which summarizes the factors assessed above, as well as their clinical applicability.

Evaluated end-points

The primary objective of our review was the pregnancy rate after tubal anastomosis. Secondary objective included other outcomes such as live birth rate, pregnancy rate by age, and pregnancy rate by years between sterilization and anastomosis, and unfavorable outcomes such as fetal loss and ectopic pregnancies rate. We also evaluated clinical characteristics of our population, such as age, body mass index (BMI), type of TL, time between TL and anastomosis, reason for re-anastomosis, length of hospital stay according to the surgical approach, and duration of surgery, which could potentially affect the pregnancy rate after tubal re-anastomosis.

Finally, we wanted to compare the results of age-stratified success rate after IVF for tubal factor infertility with the success rate after agestratified tubal anastomosis. As there were no data on age-stratified birth rates after anastomosis, we decided to subtract the sum of the overall ectopic pregnancy rate and global abortion rate from the result of the age-stratified pregnancy rate. We called this result "estimated age-stratified birth rate". These data were compared to data obtained from the Centers for Disease Control and Prevention (CDC) in the United States, where the results of birth rates after embryo transfer to patients who used their own eggs and underwent IVF due to tubal factor infer-tility are compiled.

Statistical analysis

Each available comparison, expressed as a proportion with a 95 % confidence interval (CI), was calculated using a random-effects metaanalysis. Statistical heterogeneity was assessed using the I^2 test, by the DerSimonian and Laird method. Patient characteristics were calculated using weighted means based on the study's sample size, and their dispersion was expressed using the range of values obtained (lower and upper values), as there were no measures of dispersion in most of these results. Stata 16 [33] was used as the statistical software for conducting the statistical analysis and generating graphs.

Publication bias was assessed using a funnel plot, which plots the effect size (standard error on the X-axis) against the main measure of precision (post-surgical pregnancy rate on the Y-axis).

Results

Study selection

The first search strategy yielded 359 results, of which 22 studies were included: 16 retrospective cohort studies, 7 case series, 3 case-control studies, and 2 reviews (Fig. 1). After limiting the search to publication dates between January 2012 and June 2022 and adding language and sample size restrictions, 327 studies were removed. Beyond that, 10 studies were rejected as individual cases, opinion articles, or studies found to be duplicated in other publications. After the final selection, 22 studies that fulfilled the inclusion criteria were selected for review.

The search strategy found no randomized controlled trials. From the 22 studies included, a total of six studies compared different surgical techniques assessing different surgical approaches, three compared laparoscopic with laparotomic microsurgical approaches; one study compared robotic with laparoscopic microsurgical techniques, three studies compared all three techniques simultaneously and all studies reported pregnancy rate as the primary outcome.

Since no randomized controlled trials were found comparing laparotomic microsurgical, laparoscopic, and robotic techniques, results will be described separately for each technique (Tables 2 and 3).

Patient characteristics

Study sizes were very heterogeneous, with an average of 639 women per study (range 10–10,719). In all studies, the duration of follow-up was at least 6 months (see Table 1).

The mean age of women who underwent the intervention was 34.4 years (n = 3187, range = 28.9–42.7), calculated from studies that reported this information. The mean body mass index (BMI) was 23.5 (n = 1428, range = 21.0-29.0) kg/m² and the mean time between sterilization and tubal anastomosis was 6.9 years (n = 2708, range = 4.3-9.2).

Among the studies that included information on the different types of tubal sterilization procedures undergone by women (n = 1316), it was observed that the most common modality was the use of clips or sterilization rings (40.2 %), followed by the surgical technique of section and ligation (20.9 %). The technique of electrocoagulation was used in 2.7 % of cases, while others did not specify the technique used for the sterilization (36.2 %).

The reasons that led the patients to undergo this type of reintervention were identified. In the studies that collected this data (n =

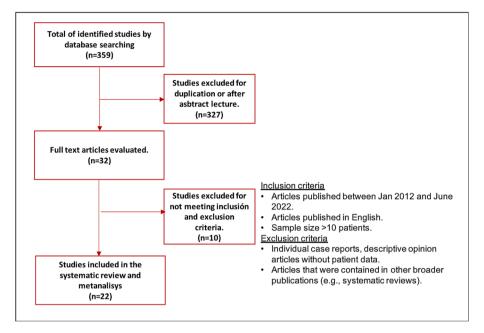


Fig. 1. Flowchart of the process for identifying, screening, and including studies in the review.

Table 1	
Patients	characteristics.

v (vears), mean (ra	nge)
(28.9–37.7)	N = 3187
(21.0-29.0)	N = 1428
iean (range)	
(4.3–9.2)	N = 2708
316)	
529	(40.2 %)
275	(20.9 %)
36	(2.7 %)
476	(36.2)
39)	
577	(43.1 %)
414	(30.9 %)
305	(22.8 %)
131	(9.8 %)
82	(6.1 %)
ording to approacl	1, min (range)
154.3	(148,7–168,0)
170.3	(104,2–201,9)
108.1	(60.0-214.7)
ording to approacl	ı, min (range)
2.0	(1.3-2.6)
1.7	(1.6–1.8)
1.9	(1.7–3.5)
	(21.0-29.0) nean (range) (4.3-9.2) 316) 529 275 36 476 39) 577 414 305 131 82 cording to approach 154.3 170.3 108.1 cording to approach 2.0 1.7

1339), it was observed that the most prevalent reason was a new marriage or new partner (43.1 %). This reason was followed by the desire to expand the offspring after the ligation (30.9 %), the death of a child (22.8 %), reasons of conscience (9.8 %), and other unspecified reasons (6.1 %).

Regarding the tubal anastomosis procedure, the three most common types of surgical approach for this type of intervention were differentiated: laparotomy, minimally invasive surgery (laparoscopy or roboticassisted), and data on the duration of surgery and length of hospital stay were obtained according to the type of surgical approach. Depending on the approach used, surgery lasted 154.30 min (148.7–168.0) for laparotomy (n = 262), 170.3 min (104.2–201.9) for laparoscopy (n = 201), and on average 108.1 min (60.0–214.7) for robotic-assisted surgery (n = 418). The length of hospital stay after surgery also varied depending on the type of approach, being 1.9 days for laparotomy (n = 78), 1.7 for laparoscopic surgery (n = 78), and 1.9 for robotic-assisted surgery (n = 124). No statistically significant differences were found between the duration of surgeries or hospitalization days.

Sufficient data was not obtained to calculate the average economic cost of each type of intervention according to the approach.

Pregnancy rate after tubal reversal

Laparotomy approach

A total of nine studies [8,10–21] were found that reported on the outcomes of tubal sterilization reversal through laparotomy. In individual studies, this technique resulted in pregnancy rates ranging from 34.5 % to 85.1 %. When all patients were pooled together, the pregnancy rate was 62.4 % (95 % CI: 54.9–70.5 %; n = 11153). Only three studies reported on the live birth rate giving results of 18.64 %, 28.57 and 38.50 %. +. Laparotomy-based sterilization reversal is associated with a risk of ectopic pregnancies of 6.0 % (95 % CI: 1.8–10.2 %).

Laparoscopic approach

The effectiveness of laparoscopic sterilization reversal was found in twelve studies assessed [8,11,16–18,21–24,32]. Individual studies reported pregnancy rates ranging from 55.2 % to 75.3 %, with a combined pregnancy rate of 67.1 % (95 % CI: 63.8–70.5 %; n = 1340). The overall rate of ectopic pregnancies was 6.8 % (95 % CI: 3.4–10.1 %). Postsurgical live birth rate was only reported in eight studies with a result that oscillated between 32.6 % and 58.3 %.

Robotic-assisted surgery

Finally, six studies [4,7–8,16,25–26] utilized robotic-assisted surgery for sterilization reversal. Pregnancy rates following robotic-assisted laparoscopic surgery ranged from 59 % to 78 %, with a combined pregnancy rate of 66.6 % (95 % CI: 58.4–74.7 %; n = 599). The combined rate of ectopic pregnancy was 8.7 % (95 % CI: 2.9–14.6 %). Live birth rates were only reported in two studies (40 % and 42 %).

Global outcomes

Pregnancy rates from 14,113 patients were obtained from individual studies and combined, resulting in an overall pregnancy rate of 65.3 %

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Study Date n	Date	n	Patients characteristics		Reason for the surgery					Type of sterilization					Length of hospitalization according to approach			Duration of the surgery		
		Mean age (years)	BMI (kg/ m2)	Time between tubal ligation and anastomosis (years)	Desire for a new child	Ethical/ moral	Deceased child	New partner	Not specified	Surgical ligation	Clips/ rings	Electrocoagulation	Others	LPT	LPC	RX	LPT	LPC	RX	
Lian C, et al.	may- 22	247	35.7		8.4			64.4 %	28.3 %	5.8 %										
Elci G, et al.	sept- 22	236	33.3	24.4	6.6										1.9 ±	1.6 ±	1.7 ±	$\begin{array}{c} 168.1 \\ \pm \ 30.1 \end{array}$	$\begin{array}{c} 177.8 \\ \pm \ 21.9 \end{array}$	$\begin{array}{c} 214.7 \pm \\ 20.5 \end{array}$
Ghomi A, et al.	aug- 20	109	36	29											0.7	0.6	0.4			60.0 ± 9.
Barac S, et al.	20 may- 20	185	31.8								87.5 %			12.5 %						72 ± 42
Chua KH, et al.	apr- 20	12	34	23.4							16.7 %	75.0 %		8.3 %					$\begin{array}{c} 156 \ \pm \\ 20 \end{array}$	
Godin PA, et al.	jan- 19	93	37.5								7.5 %	49.4 %	43 %							
Yapca OE, et al.	nov- 17	52	34.6		5	57.7 %	11.5 %	3.9 %	5.8 %											
Maskens M, et al.	jan- 18	23	35.6		5.4							100 %				1.8 \pm 0.4			104.2 ±	± 26.4
Karayalcin R, et al.	jan- 18	24	31.8		5.1	20.8 %		20.8 %	66.7 %											
Jamwal S, et al.	may- 17	23						80.0 %	12.0 %	8.0 %									$\begin{array}{c} 105 \pm \\ 20 \end{array}$	
van Seeters JAH, et al.	mar- 17	10,719																		
Park JH, et al.	may- 16	11	28.8	21.0													3.5 \pm 0.8			$\begin{array}{c} 194.6 \pm \\ 31.3 \end{array}$
Yadav R, et al.	jan- 16	36	36.01	28.7	6.8												0.0			
Malacova E, et al.	oct- 15	969	33		4.9							50.7 %		51.4 %						
Rizvi S, et al.	dec- 15	59	33.3								96.6 %	3.3 %								
la Grange J, et al.	apr- 13	184																$\begin{array}{c} 148.7 \\ \pm \ 32.5 \end{array}$	$\begin{array}{c} 201.9 \\ \pm \ 33.8 \end{array}$	
Monteith CW, et al.	dec- 14	70	37		4.3															
Huijgens ANJ, et al.	apr- 14	19	33.2		6.2		5.0 %	5.0 %	74.0 %	16.0 %		100 %								
Çetin C, et al.	jan- 13	58	30.5	26.8	6.4															
Göçmen A, et al.	jan- 13	10	37.7	28.9													1.2			130.6 (102–16
Sreshthaputra O, et al.	mar- 13	88	34.7		9.2			12.0 %	84.0 %	4.0 %	90.0 %			10.0 %				$\begin{array}{c} 158 \ \pm \\ 53 \end{array}$		
Moon HS, et al.	feb- 12	886	36.1	22.1	9	42.8 %		12.3 %	44.9 %											

BMI: body mass index; LPT: laparotomy; LPC: laparoscopy; RX: robot-assisted surgery.

Table 3 Results of the research (2).

Study	Date	n	Postop pregna	erative ncy rate		Birth ra	ite		Postope rate	erative a	bortion	Ectopic	pregnar	ncy rate	Pregnancy	rate by age	e		years b	•	ccording to erilization
			LPT	LPC	RX	LPT	LPC	RX	LPT	LPC	RX	LPT	LPC	RX	< 30 years	30–35 years	36–39 years	\geq 40 years	<5 years	5–9 years	≥10 years
Lian C, et al.	may- 22	247	66.3 %	67.9 %																	
Elci G, et al.	sept- 22	236	52.6 %	67.3 %	61.2 %	38.5 %	50.9 %	46.6 %	10.3 %	9.1 %	11.7 %	3.8 %	3.6 %	2.9 %	71.2 %	57.1 %			76.3 %	55.2 %	40.0 %
Ghomi A, et al.	aug-20	109			59.0 %												44.0 %	45.0 %			
Barac S, et al.	may- 20	185			78.0 %									8.5 %			56.7 %	33.3 %			
Chua KH, et al.	apr-20	12		75.0 %			58.3 %						11.1 %								
Godin PA, et al.	jan-19	93		75.3 %			52.7 %			2.9 %			8.6 %				77.5 %	68.4 %			
Yapca OE, et al.	nov-17	52					32.6 %			13.5 %			7.7 %			57.9 %			58.8 %		
Maskens M, et al.	jan-18	23		66.6 %			44.0 %			12.0 %			4.0 %		100.0 %	42.8 %		66.6 %			
Karayalcin R, et al.	jan-18	24		55.5 %									3.7 %								
Jamwal S, et al.	may- 17	23		64.0 %			56.0 %			8.0 %									64.0 %		
van Seeters JAH, et al.	mar-17	10,719	68.0 %	65.0 %	65.0 %							10.4 %	5.6 %	15.0 %							
Park JH, et al.	may- 16	11			63.6 %						9.0 %										
Yadav R, et al.	jan-16	36	69.0 %	71.4 %					13.8 %			3.4 %	14.3 %								
Malacova E, et al.	oct-15	969					52.0 %								61.1 %	63.1 %	27.7 %				
Rizvi S, et al.	dec-15	59	34.5 %			18.6 %			8.5 %			5.1 %			75.0 %	45.5 %	21.4 %				
la Grange J, et al.	apr-13	184	71.3 %	74.4 %								7.4 %	7.8 %								
Monteith CW, et al.	dec-14	70	44.3 %			28.6 %			11.4 %												
Huijgens ANJ, et al.	apr-14	19		63.2 %			47.0 %			25.0 %			8.0 %								
Çetin C, et al.	jan-13	58		55.2 %									1.7 %								
Göçmen A, et al.	jan-13	10			70.0 %			40.0 %			10.0 %			10.0 %							
Sreshthaputra O, et al.	mar-13	88	62.5 %						16.0 %			9.0 %									
Moon HS, et al.	feb-12	886	85.1 %						8.6 %			2.5 %			97.5 %	92.4 %		53.9 %			

LPT: laparotomy; LPC: laparoscopy; RX: robot-assisted surgery.

(95 % CI: 61.0-69.6) following reversal of TL (Fig. 2).

The percentage of women who had at least one live birth, i.e., the birth rate, was calculated to be 42.6 % (95 % CI: 34.9–51.4).

The adverse outcomes following surgery were also studied. The observed abortion rate among women undergoing surgery was 9.4 % (95 % CI: 7.0–11.7), and the overall ectopic pregnancy rate was 6.8 % (95 % CI: 4.6–9.0) (Fig. 3).

Comparations among techniques

Pregnancy rates for the three different surgical techniques, laparotomy, laparoscopy, and robotic surgery, showed no statistical significant difference were found (Fig. 2).

Stratifying the result of ectopic pregnancy rate by the type of surgical approach did not yield statistically significant differences (Fig. 3).

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Prognostic factors

The prognostic factors that were most commonly described in the included studies were investigated, such as age, BMI, time between sterilization and re-anastomosis, type of sterilization, reason for surgery, duration of anastomosis, or length of hospital stay. Relevant data could only be obtained for age and the period of time between sterilization and anastomosis.

According to most studies, age was identified as the most important and influential prognostic factor. Nine different studies stratified The pregnancy rate into age groups (n = 2671). For women under 30 years old, the pregnancy rate was 76.3 % (95 % CI: 53.0–99.5); for those between 30 and 35 years old, the rate was 60.6 % (95 % CI: 42.8–78.4); for women between 36 and 39 years old, the pregnancy rate was 59.4 % (95 % CI: 41.4–77.5); and for those 40 years old or older, the pregnancy rate was 52.4 % (95 % CI: 40.7–64.0) (Fig. 4).

o			Proportion	
Study	Year	n	(95% CI)	Weig
Laparotomy				
Lian C, et al.	2022	113	0.66 (0.58, 0.75)	4.5
Elci G,et al.	2022	78	0.53 (0.37, 0.68)	3.2
van Seeters JAH,et al.	2017	9734	0.68 (0.67, 0.69)	5.0
Yadav R,et al.	2016	29	0.69 (0.52, 0.86)	3.0
Rizvi S, et al.	2015	59	0.34 (0.22, 0.47)	3.8
la Grange J, et al.	2013	96	0.71 (0.62, 0.80)	4.
Monteith CW, et al.	2014	70	0.44 (0.33, 0.56)	3.
Sreshthaputra O, et al.	2013	88	0.63 (0.52, 0.73)	4.
Moon HS, et al.	2012	886	0.85 (0.83, 0.87)	5.
Subgroup, DL (I ² = 96.6%	, p = 0.000)		0.62 (0.54, 0.71)	38.8
Laparoscopy				
Lian C, et al.	2022	134	0.68 (0.59, 0.76)	4.
Elci G, et al.	2022	55	0.67 (0.52, 0.82)	3.
Chua KH, et al.	2020	12	0.75 (0.51, 0.99)	1.
Godin PA, et al.	2019	93	0.75 (0.67, 0.84)	4.
Maskens M, et al.	2018	23	0.67 (0.47, 0.86)	2.
Karayalcin R, et al.	2018	24	0.56 (0.36, 0.75)	2.
Jamwal S, et al.	2017	23	0.64 (0.44, 0.84)	2.
van Seeters JAH, et al.	2017	804	0.65 (0.62, 0.68)	5.
Yadav R, et al.	2016	7	0.71 (0.38, 1.05)	1.
a Grange J, et al.	2013	88	0.74 (0.65, 0.84)	4.
Huijgens ANJ, et al.	2014	19	0.63 (0.42, 0.85)	2.
Çetin C, et al.	2013	58	0.55 (0.42, 0.68)	3.
çetin C, et al. Subgroup, DL (I ² = 13.3%	p = 0.315)		0.67 (0.64, 0.71)	39.
Robotic	,			
Elci G, et al.	2022	103	0.64 (0.40.0.72)	3.
Ghomi A, et al.	2022	103	0.61 (0.49, 0.73) 0.59 (0.50, 0.68)	3. 4.
	2020	185	0.78 (0.72, 0.84)	5.
Barac S, et al.	2020	181	0.78 (0.72, 0.84)	4.
van Seeters JAH, et al.	2017	181	0.65 (0.58, 0.72)	4. 1.
Park JH, et al.	2017	10		1.
Göçmen A, et al.		10	0.70 (0.42, 0.98)	21.
Subgroup, DL (I ² = 69.4%	, p = 0.006)		0.67 (0.58, 0.75)	21.
Heterogeneity between gr		05		
Overall, DL (l ² = 90.4%, p	= 0.000)		0.65 (0.61, 0.70)	100.0

Fig. 2. Forest plot: pregnancy rate according to surgical approach. The main outcome (pregnancy rate) is stratified according to whether the surgical approach was by laparotomy, laparoscopy, or robotically assisted surgery. Each result is given with a 95%CI and the heterogeneity is calculed with the I² test (DL: DerSimonian and Laird method).

Study	Veee		Proportio
	Year	n	(95% C
Laparotomy			
Elci G,et al.	2022	78	0.04 (-0.02, 0.10)
van Seeters JAH,et al.	2017	9734	• 0.10 (0.10, 0.11)
Yadav R,et al.	2016	29	0.03 (-0.03, 0.10)
Rizvi S, et al.	2015	59	0.05 (-0.01, 0.11)
la Grange J, et al.	2013	96	0.07 (0.02, 0.13)
Sreshthaputra O, et al.	2013	88	0.09 (0.03, 0.15)
Moon HS, et al.	2012	886	 0.03 (0.01, 0.04)
Subgroup, DL (l ² = 96.6%, p =	0.000)		0.06 (0.02, 0.10)
Laparoscopy			
Elci G, et al.	2022	55	0.04 (-0.02, 0.10)
Chua KH, et al.	2020	12	0.11 (-0.07, 0.29)
Godin PA, et al.	2019	93	0.09 (0.03, 0.14)
Yapca OE, et al.	2018	52	0.08 (0.00, 0.15)
Maskens M, et al.	2018	23	0.04 (-0.04, 0.12)
Karayalcin R, et al.	2018	24	0.04 (-0.04, 0.11)
van Seeters JAH, et al.	2017	804	0.06 (0.04, 0.07)
Yadav R, et al.	2016	7	0.14 (0.12, 0.17)
la Grange J, et al.	2013	88	0.08 (0.02, 0.13)
Huijgens ANJ, et al.	2014	19	0.08 (-0.04, 0.20)
Çetin C, et al.	2013	58	0.02 (-0.02, 0.05)
Subgroup, DL (l ² = 82.6%, p =	0.000)		0.07 (0.03, 0.10)
Robotic			
Elci G, et al.	2022	103	0.03 (-0.01, 0.07)
Barac S, et al.	2020	185	0.09 (0.05, 0.13)
van Seeters JAH, et al.	2017	181	0.15 (0.10, 0.20)
Göçmen A, et al.	2013	10	0.10 (-0.09, 0.29)
Subgroup, DL (I ² = 76.7%, p = 0	0.005)		0.09 (0.03, 0.15)
Heterogeneity between groups:	p = 0.759		
Overall, DL (l ² = 91.5%, p = 0.0	00)		0.07 (0.05, 0.09)

Fig. 3. Forest plot: ectopic pregnancy rate according to surgical approach. The main outcome (ectopic pregnancy rate) is stratified according to whether the surgical approach was by laparotomy, laparoscopy, or robotically assisted surgery. Each result is given with a 95%CI and the heterogeneity is calculed with the I^2 test (DL: DerSimonian and Laird method).

Results from nine studies were obtained for the pregnancy rate according to the period of time between sterilization and anastomosis. Patients who had been sterilized for less than 5 years had a pregnancy rate of 68.3 % (95 % CI: 56.7–79.9); those who had been sterilized for 5–9 years had a pregnancy rate of 55.2 % (95 % CI: 48.7–61.6); and those who had been sterilized for 10 years or more had a pregnancy rate of 40.0 % (95 % CI: 33.6–46.3).

Sterilization reversal versus IVF

After comparing data based on 13,970 IVF cycles performed in 2019 [27], it was found that the percentage of transfers resulting in live births was, depending on age, 52.7 % for those under 35 years old; 31.2 % for women between 35 and 40 years old; and 7.9 % for those over 40 years old. There are no data that stratify the results for those under 30.

The result of the "estimated age-stratified birth rate" was 60.1 % for women under 30 years old. The estimated birth rate for women between 30 and 35 years old was 44.4 %. For women between 35 and 40 years old, the result was 43.2 %. Finally, the estimated birth rate for women over 40 years old was 36.2 %. These data can be compared in Fig. 5.

Discussion

After analyzing the results of 22 studies containing information from 14,113 women that evaluated the three most commonly used techniques for tubal anastomosis after sterilization through ligation, it has been shown that the overall pregnancy rate after anastomosis is 65.3 % (95 % CI: 61.0–69.6), a hopeful result for women who want to opt for this technique to recover fertility. Pregnancy rates were similar regardless of the technique used, however, the surgical approach most commonly used is minimally invasive surgery, which offers a faster recovery but requires a higher level of surgical training and experience.

The mean age of the women studied was 34.4 years, an age at which fertility is not the same as in younger women, with an adequate mean BMI of 23.6 kg/m^2 on average. The most common type of ligation among the women studied was tubal occlusion using clips or rings.

		Proportion	%
Study	Year	(95% CI)	Weight
<30 years			
Elci G,et al.	2022	0.71 (0.65, 0.77)	5.74
Malacova E, et al.	2015	0.61 (0.58, 0.64)	5.82
Rizvi S, et al.	2015	0.75 (0.64, 0.86)	5.47
Moon HS, et al.	2012	 0.98 (0.96, 0.99) 	5.85
Subgroup, DL (I ² = 99.	5%, p = 0.000)	0.76 (0.53, 1.00)	22.88
30-35 years			
Elci G,et al.	2022	0.57 (0.51, 0.63)	5.72
Yapca OE, et al.	2018	0.58 (0.44, 0.71)	5.30
Maskens M, et al.	2018	0.43 (0.23, 0.63)	4.73
Malacova E, et al.	2015	0.63 (0.60, 0.66)	5.82
Rizvi S, et al.	2015	0.46 (0.33, 0.58)	5.35
Moon HS, et al.	2012	• 0.92 (0.91, 0.94)	5.84
Subgroup, DL ($I^2 = 98$.	8%, p = 0.000)	0.61 (0.43, 0.78)	32.77
36-39 years			
Ghomi A, et al.	2020	0.44 (0.35, 0.53)	5.57
Barac S, et al.	2020	0.57 (0.50, 0.64)	5.69
Godin PA, et al.	2018	0.77 (0.69, 0.86)	5.62
Subgroup, DL (I ² = 93.	0%, p = 0.000)	0.59 (0.41, 0.77)	16.88
≥40 years			
Ghomi A, et al.	2020	0.45 (0.36, 0.54)	5.57
Barac S, et al.	2020	0.33 (0.27, 0.40)	5.70
Godin PA, et al.	2018	0.68 (0.59, 0.78)	5.57
Maskens M, et al.	2018	0.67 (0.47, 0.86)	4.82
Moon HS, et al.	2012	.54 (0.51, 0.57)	5.82
Subgroup, DL (I ² = 91.	3%, p = 0.000)	0.52 (0.41, 0.64)	27.47
Heterogeneity between	n groups: p = 0.340		
Overall, DL (I ² = 99.2%	6, p = 0.000)	0.62 (0.52, 0.72)	100.00

Fig. 4. Forest plot: pregnancy rate stratified by age. The main outcome (ectopic pregnancy rate) is stratified according to whether the surgical approach was by laparotomy, laparoscopy, or robotically assisted surgery. Each result is given with a 95%CI and the heterogeneity is calculed with the I² test (DL: DerSimonian and Laird method).

Interestingly, the most common reason was a new marriage or the start of a new relationship. We concluded that the factor with the strongest prognostic value was age.

The choice to select between IVF or TL reversal is mainly based on the patient's preference. Surgical re-anastomosis of the fallopian tubes has the advantage that if the woman desires, she can attempt pregnancy again without undergoing another cycle since tubal function is restored. At the same time, women undergoing IVF have to undergo additional treatment. The surgery also has the advantage that women are more psychologically at ease knowing that they are fertile again [16].

Furthermore, after the restoration of fertility through tubal recanalization, the risk of multiple pregnancies is the same as that of a woman with a spontaneous pregnancy. However, it is known that compared to IVF, women who transfer multiple embryos are at risk of developing a multiple pregnancy, and at the same time, there is a high risk of premature birth, preeclampsia, and gestational diabetes [28].

Beyond the personal preferences of the patients, the cost disparity between these two techniques can influence patients when making their choice. In Spain, the price of IVF can fluctuate depending on the clinic and location, with costs typically ranging from 3000 to 7000 euros per cycle. On the other hand, the cost of tubal ligation reversal at centers like ours is approximately 5000 euros.

The rate of abortions in the literature following tubal anastomosis is similar to that published in the context of spontaneous abortion by the World Health Organization (WHO) [29], which is in the range of 10 to 20 %. On the other hand, the rate of ectopic pregnancy in the population after anastomosis was 6.9 %, which is higher than in the general population (ectopic pregnancy rate of 1–2 %). However, it should be noted that the ectopic pregnancy rate in the infertile population can reach 7 % according to the Spanish Fertility Society, underscoring that the condition of infertility increases the risk of experiencing an extrauterine pregnancy [30]. However, this data deviates from the percentage of ectopic pregnancies that occur following the utilization of IVF techniques, reaching a rate of 2 % according to the CDC. Therefore, surgery could potentially lead to an increase in the ectopic pregnancy rate in these patients.

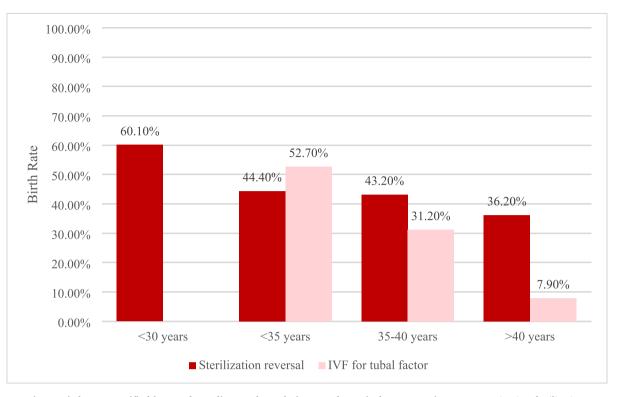


Fig. 5. Birth rate stratified by age depending on the technique used: surgical anastomosis or IVF. IVF: in vitro fertilization.

The results of the pregnancy rate according to the period of time between sterilization and anastomosis can be explained not only because the fallopian tubes suffer chronic damage from ligation, but also because those that had a longer time since sterilization are more likely to be older.

When comparing the results of IVF with TL reversal, reversal procedures seem more favorable for patients over 35 years old, while results are similar for patients under 35 years old. However, currently, there is a lack of data on both age-stratified birth rates in patients undergoing the studied intervention and outcomes of young women undergoing IVF, as only the joint data of those under 35 years old is available.

Strengths and limitations

Among the strengths of this study, it is worth highlighting that it is the most exhaustive, updated, and complete literature review of the last 10 years. The previous review was conducted in 2017 [16] and included approximately 9000 patients, whose results did not differ from those found in this publication, finding a pregnancy rate between 42 and 69 %. This study includes a very significant number of patients, providing very extensive information that had never been previously gathered. Another strength of our study has been the evaluation of a possible publication bias. The funnel plot (Fig. 6) shows that no publication bias has been found, meaning that publications with low pregnancy rates do not go unpublished.

Finally, the data found are consistent with those previously published in the last decade in the literature, which adds robustness to the success rates of this intervention, showing relevant and solid results.

The main limitation of this study is that it includes a retrospective analysis of heterogeneous observational series with the absence of clinical trials. Objectively, in retrospective studies, bias is higher, and the level of evidence is lower.

Another weakness of the review is that, within the reviewed publications, various groups usually have a similar approach when performing the anastomosis. Exceptionally, in some studies, attempts were made to compare results between different techniques performed by the

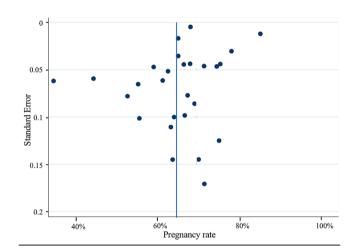


Fig. 6. Funnel plot. Effect size (standard error on the X-axis) against the main measure of precision (post-surgical pregnancy rate on the Y-axis).

same group. However, when dividing the sample and reducing it, the results were undervalued or overvalued, making it impossible to obtain reliable results within the groups that performed the technique with different approaches. Likewise, the sample size of many of the selected studies was small, and the average age of women in some of them was high, causing the success rate of those studies to be lower than the rest and causing the range of dispersion measures to be wider.

It should also be noted that the follow-up protocols for these patients in different studies follow very heterogeneous criteria, and it is not clear in most studies the percentage of patients lost after the anastomosis or the time of follow-up of the women after surgery. Similarly, in most studies, the choice of surgery type depended on the surgeon, being a choice based on convenience or experience, making the possibility of masking null or almost null.

The pregnancy rate could have also been calculated for unilateral

versus bilateral tubal anastomosis. Similarly, the success rate could have been stratified based on post-reanastomosis tubal length. The results based on the follow-up time of the patients were very limited, therefore the main data could not be adjusted to this factor.

Finally, another limitation of the research is the absence in the publications of the factual data on the age-stratified birth rate, which has forced the design of a weighted rate, calculated from the percentage of pregnancies, abortions, and ectopic pregnancies. Perhaps the calculated result may deviate from the real value, but it is the most approximate data that can be reached with the information available if compared to the post-in vitro fertilization birth rate.

Conclusion

In this systematic review on tubal re-anastomosis surgery, we demonstrated that it is an effective technique for restoring fertility in women who have previously undergone TL, despite the limited number of suitable studies we found. We were able to compare success rates between different surgical approaches without finding significant differences. The factor that most influences surgical outcomes is age. For older women, the data indicate that surgery has higher success rates than IVF, and in younger women, the results are similar; however, more data and randomized trials are needed to make this assertion. The available literature review demonstrates that surgical anastomosis after TL is a reproducible technique with relevant success rates, carried out by multiple groups of experts worldwide.

Disclosure statement

I attest that all authors meet the International Committee of Medical Journal Editors (ICMJE).

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ejogrb.2023.10.017.

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