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Fertility-Sparing Treatment in Early-Stage Cervical Cancer: Oncologic Safety and Pregnancy Outcomes

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ABSTRACT

Cervical cancer is one of the most common cancers in women of reproductive age. As a result, fertility preservation is now considered an integral component of standard oncology care. Fertility-sparing therapy (FST) includes early-stage cervical conization and more complex surgical procedures, for example, radical trachelectomy with pelvic lymph node evaluation. For patients with larger tumors, neoadjuvant chemotherapy (NACT) is being investigated as an experimental option before fertility-sparing surgery. This review summarizes current evidence on the safety and reproductive outcomes associated with FST in patients with early-stage cervical cancer. We searched PubMed/MEDLINE and Google Scholar for systematic reviews, cohort studies, retrospective analyses, and clinical guidelines. Studies published within the last 10 years were prioritized. The review examines patient selection, key tumor characteristics, cancer treatment outcomes, and the possibility of having children. Current evidence shows that patients with FIGO IA1-IB1 disease, tumors 2 cm or smaller, favorable pathology, and no lymph node involvement can have cancer outcomes with FST like those after radical hysterectomy. Women who undergo FST generally achieve encouraging reproductive results, with pregnancy rates surpassing 50% in most reported series. That said, more extensive surgical interventions carry a meaningful increase in the risk of both miscarriage and premature delivery. Preliminary findings on NACT followed by fertility-sparing surgery in tumors ranging from 2 to 4 cm show promise, though larger prospective trials are still needed to better define which patients benefit most.

Keywords: Cervical cancer; Fertility preservation; Radical trachelectomy; Oncologic safety; Pregnancy outcomes

1. INTRODUCTION

Epidemiology and Biological Background

Cervical cancer is a serious health problem and is the fourth most commonly diagnosed cancer in women worldwide. In 2018, over 500,000 new cases and over 311,000 deaths were reported worldwide. In the WHO European Region,

approximately 60,000 women are diagnosed with cervical cancer each year. However, nearly 90% of deaths occur in low- and middle-income countries. This is due to differences in HPV vaccination coverage, access to screening, and timely treatment (Stelzle et al., 2021; WHO/Europe, 2025).

Prevention, early detection, and treatment have significantly improved treatment outcomes. In specialized centers, five-year survival for localized cancer exceeds 90%. This results in a growing population of long-term survivors (Willows et al., 2016; Nezhat et al., 2020). This is clinically significant because cervical cancer frequently affects women of reproductive age. Approximately 40% of cases are diagnosed in women before the age of 45. The average age of onset is approximately 47 (Habib et al., 2025). Therefore, fertility preservation has become a key aspect of care and improving quality of life for these women (Floyd et al., 2021).

High-risk HPV infection underlies virtually all cases of cervical cancer, with subtypes 16 and 18 accounting for most oncogenic events, while types 31, 33, 35, 39, 45, 51, 52, 56, 58, and 59 are also regularly identified (Stelzle et al., 2021). From a histological standpoint, squamous cell carcinoma predominates, comprising 80–90% of diagnoses. Adenocarcinoma, though less frequent, tends to present at a more advanced stage and carries a comparatively worse prognosis, in part because conventional Pap smear screening is less sensitive for its detection (Mattei et al., 2024).

When assessing a patient's eligibility for fertility-sparing treatment, tumor-related factors take center stage. The key variables guiding clinical decision-making include tumor dimensions, the depth of stromal invasion, the presence of lymphovascular space invasion (LVSI), and the histological subtype. High-grade aggressive variants (neuroendocrine carcinoma in particular) are regarded as contraindications to conservative management given their propensity for early recurrence (Habib et al., 2025).

Eligibility Criteria for Fertility-Sparing Treatment

Disease stage is assessed based on the 2018 International Federation of Gynecology and Obstetrics (FIGO) classification. In clinical trials and in accordance with international guidelines, the status of the pelvic lymph nodes is the most important prognostic factor for treatment. The presence of lymph node metastases usually precludes uterine preservation. Standard treatment relies on chemoradiotherapy, which does not guarantee future fertility (Habib et al., 2025). In the context of fertility-sparing surgery, a tumor diameter below 2 cm (FIGO IA2–IB1) is widely accepted as the threshold beyond which oncological risk becomes difficult to justify.

While LVSI raises concern for lymph node spread, it is not an automatic disqualifier. When favorable prognostic features are present and nodal staging is negative, conservative treatment remains a viable path. Conversely, histological subtypes associated with aggressive behavior - including neuroendocrine carcinoma and glassy cell carcinoma - fall outside the scope of fertility preservation (Habib et al., 2025).

Managing tumors between 2 and 4 cm in diameter (FIGO IB2) while preserving fertility remains an open and debated question. One proposed approach involves administering neoadjuvant chemotherapy before conservative surgery with the aim to achieve tumor downstaging. Solid prospective evidence to support this strategy is still lacking. However, ongoing trials such as CONTESSA/NEOCON-F are working to establish clear selection criteria and demonstrate acceptable oncological safety (Mattei et al., 2024; Silvestris et al., 2022).

Fertility-Sparing Treatment Modalities

In carefully selected patients, fertility preservation can be achieved using a variety of surgical and supportive methods. Cervical conization is considered the definitive treatment for stage IA1 cancer without LVSI and for selected low-risk lesions. It is performed using cold knife excision or electrosurgical snare excision. Reported conception rates after this treatment range from approximately 36% to 55%. Simple trachelectomy is gaining recognition as an appropriate surgical option for lower-risk IA2-IB1 tumors. The procedure entails the removal of the cervix while leaving the parametria intact, and available data consistently indicate that less radical approaches yield more favorable reproductive and obstetric outcomes than their more extensive counterparts (Habib et al., 2025; Floyd et al., 2021).

Radical trachelectomy involves the removal of the cervix together with the parametria and the upper vaginal cuff and is routinely performed alongside pelvic lymph node assessment. It is most indicated for IA2–IB1 tumors not exceeding 2 cm. When performed via the vaginal route, pregnancy rates above 65% have been reported, though the choice of approach is ultimately guided by the patient's anatomy and the surgeon's experience (Nezhat et al., 2020; Habib et al., 2025; Mattei et al., 2024).

Neoadjuvant chemotherapy has been studied as a strategy to facilitate fertility-sparing surgery in selected patients with tumors 2–4 cm in diameter. Commonly used treatment regimens include combinations such as cisplatin and paclitaxel, as well as TIP/TEP

protocols including paclitaxel, cisplatin, ifosfamide, or etoposide. Systematic reviews have shown that the pregnancy rate among women trying to conceive using this method is as high as 84.8%. Interpretation of these data is limited due to heterogeneity and selection bias (Burbano et al., 2021).

Women who require pelvic irradiation may be offered ovarian transposition (oophoropexy) as a means of shielding the ovaries from radiation and maintaining endocrine function. While success rates in preserving hormonal activity exceed 60%, natural conception is frequently compromised after this procedure, and most women will ultimately require assisted reproductive technology (ART) to achieve pregnancy (Mattei et al., 2024; Tanase et al., 2023; Angarita et al., 2016).

Other fertility preservation strategies in cancer treatment include cryopreservation of oocytes and embryos. This is currently considered the gold standard when treatment time allows. In clinical emergencies, cryopreservation of ovarian tissue may also be considered. Uterine transplantation remains experimental but may be a future option for restoring pregnancy potential for women in whom no other option remains (Angarita et al., 2016; Holland et al., 2015; Woessner et al., 2015).

2. REVIEW METHODS

We carried out a structured narrative review, following a PRISMA-based approach for literature identification and study selection. We searched PubMed/MEDLINE and Google Scholar from January to March 2026, using the following keyword strings: “cervical cancer”, “fertility-sparing therapy”, “fertility-sparing surgery”, “trachelectomy”, “oncologic outcomes”, “pregnancy outcomes”, and “neoadjuvant chemotherapy”. We also reviewed reference lists of retrieved articles to capture any relevant publications not retrieved through the primary database search.

We included studies published between 2014 and 2025. Inclusion criteria included original research articles describing oncological and/or reproductive outcomes after fertility-sparing treatment in patients with early-stage cervical cancer. Selected articles included randomized controlled trials, prospective and retrospective cohort studies, observational studies, systematic reviews and meta-analyses. Exclusion criteria included case reports, conference abstracts, editorials, and publications in languages other than English. Duplicate studies, studies lacking sufficient data on oncological or reproductive outcomes, and studies focusing on advanced-stage cervical cancer were excluded. Figure 1 shows the PRISMA flow diagram of study selection.

Data were manually extracted from all eligible studies and included study design, patient characteristics, tumor stage, treatment modality, oncological outcomes, and reproductive outcomes. Due to substantial heterogeneity across studies in patient selection, surgical techniques, and outcome reporting, a qualitative narrative synthesis was conducted. No quantitative meta-analysis or pooled statistical analysis was performed.

3. RESULTS & DISCUSSION

Oncologic Outcomes

In appropriately selected patients with early-stage cervical cancer, fertility-sparing surgery achieves oncologic outcomes comparable to those of non–fertility-sparing radical procedures. Recurrence risk is strongly influenced by baseline tumor characteristics, with tumor size being the most consistent adverse prognostic factor (Table 1). Lesions measuring 2 cm or more are associated with a significantly increased risk of recurrence, regardless of the surgical approach (Floyd et al., 2021).

Table 1. Recurrence rates by technique and stage.

FSS Technique	Tumour Stage/Size	Recurrence Rate	Mortality Rate
Conization/Simple Trachelectomy (ST)	FIGO IA1/IA2 (Low-Risk)	3.6%, 2.3%, 0.4%	0.8%
Vaginal Radical Trachelectomy (VRT)	FIGO IA2/IB1 (≤2 cm)	4.2%, <5%	1.7%, 2.5%
Abdominal Radical Trachelectomy (ART) (Laparotomy)	FIGO IA2/IB1 (≤2 cm)	3.1%	1.5%
Minimally Invasive Surgery (MIS-RT) (Lap/Robotic)	FIGO IA2/IB1 (≤2 cm)	4.5%	1.5%
NACT followed by FSS	FIGO IB2 (>2 cm)	6.3% (crude), 12.8% (systematic review)	1.3% (crude), 2.8% (systematic review)

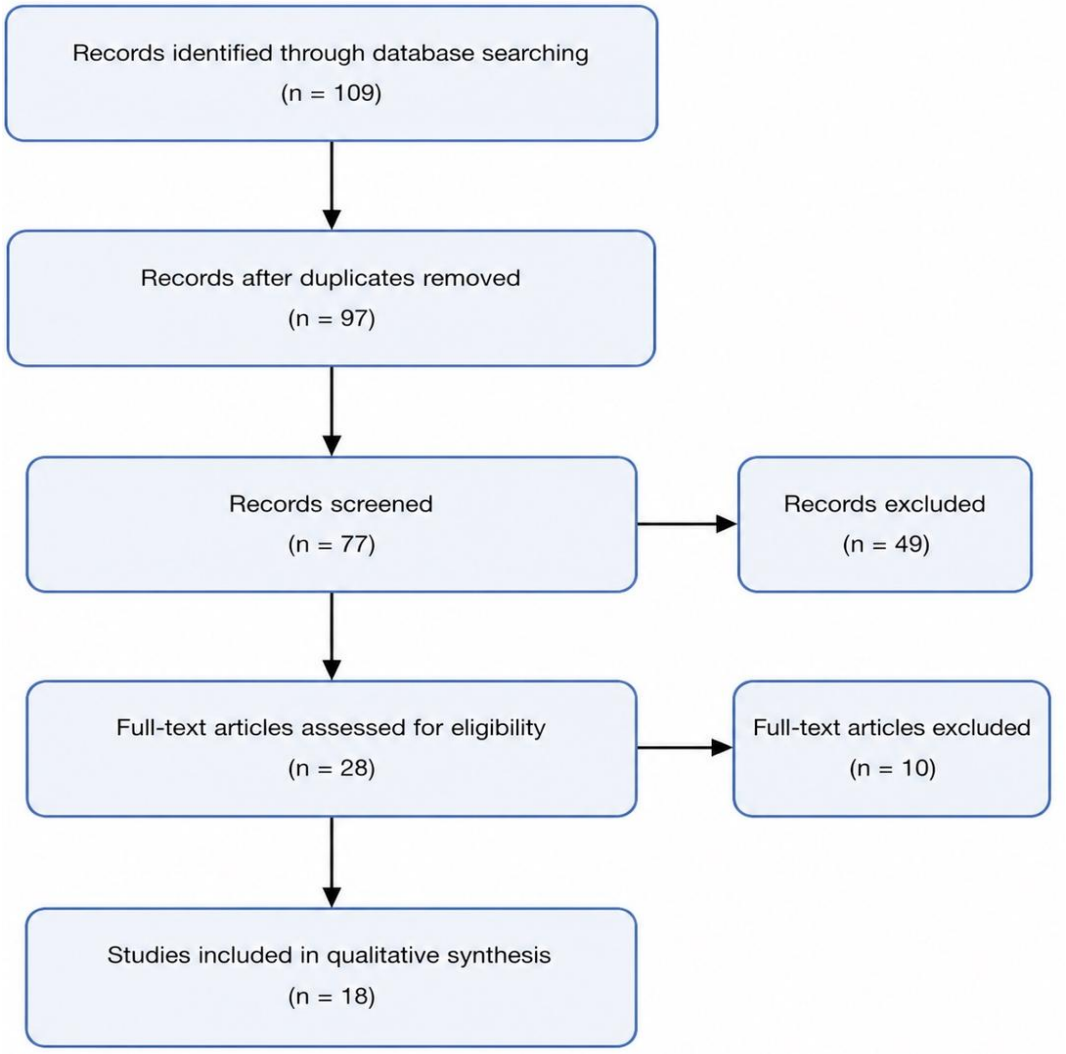

Figure 1. PRISMA flow diagram of study selection.

Recurrence risk in patients undergoing fertility-sparing procedures is shaped both by the extent of surgical resection and by intrinsic tumor characteristics (Habib et al., 2025;Schuurman et al., 2021). Primary radical trachelectomy carries a comparatively elevated recurrence burden - crude rates of up to 20.5% have been reported following vaginal radical trachelectomy and up to 18.9% after minimally invasive abdominal radical trachelectomy. In contrast, when NACT precedes fertility-sparing surgery, recurrence figures appear more favorable. Systematic reviews estimate rates around 12.8%, with disease-related mortality of approximately 2.8%, for tumors exceeding 2 cm. In selected patient series, crude recurrence rates as low as approximately 6.3% have been documented. The majority of relapses are locoregional, occurring in the cervix. Distant metastatic spread, including ovarian or pulmonary involvement, is uncommon (Willows et al., 2016; Burbano et al., 2021; Schuurman et al., 2021).

For tumors measuring 2 cm or less, a substantial body of retrospective data supports the oncological equivalence of radical trachelectomy and radical hysterectomy, with no meaningful differences in recurrence or overall survival identified across carefully matched patient cohorts (Habib et al., 2025; Schuurman et al., 2021). It is important to acknowledge that this evidence base is predominantly retrospective and therefore susceptible to selection bias. Additionally, findings from the LACC trial, which demonstrated inferior survival outcomes with minimally invasive radical hysterectomy compared with open surgery in FIGO IB1 disease, have had a broader influence on surgical decision-making in fertility- sparing contexts. Although the study was not designed to directly evaluate trachelectomy (Nezhat et al., 2020; Habib et al., 2025).

In light of these constraints, contemporary clinical guidelines place considerable emphasis on rigorous patient selection. Candidates for fertility preservation are generally those with early- stage disease (confirmed by FIGO staging), a histologically favorable tumor

type, and documented absence of pelvic lymph node involvement - the latter verified through sentinel node biopsy and/or formal lymphadenectomy. Additional risk factors, including LVSI and deep stromal invasion, are carefully weighed in the decision. Pre-operative MRI is indispensable in this setting, providing reliable information on tumor size, local extension, and whether parametrial or nodal involvement is present (Habib et al., 2025; Floyd et al., 2021).

Reproductive and Obstetric Outcomes

Overall, women who undergo fertility-sparing surgery can expect reasonably positive reproductive outcomes. However, they must be counseled thoroughly about the substantially elevated risk of preterm delivery that accompanies these procedures (Terzic et al., 2023). Across the analyzed literature, the mean clinical pregnancy rate in women actively attempting conception after fertility-sparing surgery is approximately 55%. Vaginal radical trachelectomy yields the highest rates, approaching 67.5% in some series, while conization, simple trachelectomy, and minimally invasive radical abdominal trachelectomy produce broadly comparable results, averaging around 59%. Open radical abdominal trachelectomy tends to yield lower rates, around 45%, likely reflecting postoperative pelvic adhesions and reduced uterine perfusion after uterine artery ligation (Nezhat et al., 2020; Schuurman et al., 2021).

Assisted reproductive technology (ART) is frequently utilized in this patient population. Approximately 20% of pregnancies are achieved this way. Following radical trachelectomy, up to 48.6% of pregnancies are achieved using ART (Nezhat et al., 2020; Floyd et al., 2021). To facilitate adequate oncologic surveillance and early detection of recurrence, the authors recommend delaying conception, typically for up to 12 months after surgery (Nezhat et al., 2020). An important clinical consideration following fertility-sparing treatment is that the combined first- and second-trimester miscarriage rate typically ranges from 15% to 25%. The overall pregnancy loss rate after radical trachelectomy is approximately 22.4%. The second trimester pregnancy loss is relatively common and is associated with premature rupture of membranes (Willows et al., 2016; Bentivegna et al., 2016).

Preterm delivery, defined as birth occurring before 37 completed weeks of gestation, is markedly overrepresented in this patient population, affecting approximately 31% of pregnancies on average. Rates are highest after the most radical surgical procedures, reaching up to 46.2% following radical abdominal trachelectomy. In comparison, less extensive interventions such as conization and simple trachelectomy carry considerably lower rates of around 14.9%. Interestingly, pregnancies following NACT combined with fertility-sparing surgery also show a preterm birth rate of roughly 15%, suggesting that reducing surgical radicality has a meaningful protective effect on obstetric outcomes. This can be achieved by a more conservative resection or by employing chemotherapy to downsize the tumor (Tanase et al., 2023; Schuurman et al., 2021).

Prophylactic placement of a permanent cerclage is commonly performed during radical trachelectomy. However, its effectiveness is still debated. Some studies suggest that cerclage may increase the risk of ascending infection and preterm premature rupture of membranes (Nezhat et al., 2020; Bentivegna et al., 2016). After radical trachelectomy, delivery by cesarean section is generally recommended, typically scheduled between 36 and 38 weeks of gestation, to reduce the risk of cervical trauma or hemorrhage (Šimják et al., 2020).

Current Challenges and Knowledge Gaps

Expanding HPV vaccination coverage and scaling up HPV-based screening programs represent the most upstream means of shifting the distribution of cervical cancer diagnoses toward earlier stages. In turn, broadening the pool of patients who qualify for fertility-sparing rather than radical treatment (Stelzle et al., 2021; WHO/Europe, 2025; Habib et al., 2025). On the treatment side, ongoing trials (most notably CONTESSA/NEOCON-F) are directly addressing whether neoadjuvant chemotherapy can be safely and reproducibly combined with fertility-sparing surgery (Mattei et al., 2024; Terzic et al., 2023). Simultaneously, the expanding role of immunotherapy and other targeted agents in oncological practice raises legitimate questions about gonadotoxicity and the downstream impact on reproductive capacity. These concerns underline the importance of systematically incorporating fertility-related outcome measures into the design of future oncology trials (Silvestris et al., 2022; Burbano et al., 2021).

For patients in whom uterine preservation cannot be achieved through conventional surgical means, uterine transplantation represents an experimental but potentially relevant future avenue. While a handful of cases have been performed and reported, questions surrounding long-term oncological safety and the considerable risks associated with immunosuppressive therapy must be adequately resolved before broader clinical application can be considered (Angarita et al., 2016; Woessner et al., 2015; Marklund et al., 2025).

Good pregnancy outcomes after trachelectomy depend on close, multidisciplinary follow-up. Among the key recommendations: delaying conception for oncologic surveillance, often up to 12 months. Progesterone-based interventions to prevent prematurity and regular monitoring of cervical length during the second trimester may be necessary. The approach to cerclage placement is assessed on an individual basis. Screening for infections to reduce the risk of premature rupture of membranes (PPROM). Planned cesarean section is the recommended mode of delivery (Šimják et al., 2020).

Limitations

This review has several limitations worth noting. A significant proportion of the studies we analyzed were retrospective. The included studies showed considerable heterogeneity in patient selection, tumor characteristics, surgical techniques, and reported oncological and reproductive outcomes. Comparing fertility-sparing methods directly was further complicated by inconsistent follow-up periods and varying definitions of outcomes across studies. Due to substantial methodological heterogeneity across the included studies, a formal pooled statistical analysis or meta-analysis was not undertaken. The findings of this review should therefore be interpreted accordingly. Within these constraints, however, this review offers a current and clinically grounded overview of the evidence base surrounding fertility-sparing management of early-stage cervical cancer.

4. CONCLUSION

Fertility-sparing surgery represents a meaningful treatment option for women with early-stage cervical cancer who wish to retain the possibility of future pregnancy, provided they are selected with care. In patients presenting with FIGO IA1–IB1 disease, tumors no larger than 2 cm, and negative pelvic lymph nodes, oncological outcomes are broadly comparable to those achieved with radical hysterectomy. These benefits come at the cost of a heightened risk of obstetric complications, preterm birth in particular, which must be communicated clearly and addressed proactively within a multidisciplinary framework encompassing gynecological oncology, reproductive medicine, and maternal-fetal medicine. While the overall picture is encouraging, the predominantly retrospective nature of the available evidence limits the certainty that can be attributed to these conclusions and underscores the urgent need for well-designed prospective studies. This is especially important to clarify the role of neoadjuvant chemotherapy followed by fertility-sparing surgery in the management of tumors measuring between 2 and 4 cm.

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Informed consent

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Conflict of interest

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Data and materials availability

All data associated with this study will be available based on the reasonable request to corresponding author.

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