Neuro-Oncology Advances
6(1), vdae124, 2024 | https://doi.org/10.1093/noajnl/vdae124 | Advance Access date 25 July 2024

Fertility preserving techniques in neuro-oncology patients: A systematic review

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Abstract

Background. Advancements in cancer treatments have enhanced survival rates and quality of life for patients with central nervous system (CNS) tumors. There is growing recognition of the significance of fertility preservation methods. Currently, techniques, including oocyte cryopreservation and sperm cryopreservation are established. Nevertheless, oncologists may exhibit reluctance when referring patients to reproductive specialists. This review aimed to assess the best evidence for fertility preservation techniques used in patients with CNS cancers and evaluate outcomes relating to their success and complications.

Methods. Two reviewers performed a search of Pubmed, Embase, Medline, Cochrane, and Google Scholar. Papers were included if they reported at least 1 fertility preservation technique in a neuro-oncology patient. Non-English studies, editorials, animal studies, and guidelines were excluded. Meta-analysis was performed using the random effects model.

Results. Sixteen studies containing data from 237 participants (78.8% female) were included in the systematic review and meta-analysis, of whom 110 (46.4%) underwent fertility preservation techniques. All patients (100%) successfully underwent fertility preservation with 1 participant (2.9%) returning to rewarm their oocytes, embryos or sperm. On average, 17.8 oocytes were retrieved with 78%, ultimately being cryopreserved. Five (6.0%) patients successfully conceived 9 healthy-term children after utilizing their cryopreserved sperm, embryos, or oocytes. Moreover, 6 patients successfully conceived naturally or using intrauterine insemination, resulting in 7 healthy-term children.

Conclusions. Fertility preservation techniques could offer a safe and effective way for neuro-oncology patients to deliver healthy-term babies following treatment. However, further studies concerning risks, long-term pregnancy outcomes, and cost-effectiveness are needed.

Key Points

- NICE recommends the use of fertility preservation (FP) for neuro-oncology patients wishing to preserve their fertility potential.
- Neuro-oncology patients can successfully undertake FP.
- Utilizing FP, neuro-oncology patients can conceive healthy babies at term.

Cancer of the central nervous system (CNS) represents the most prevalent form of cancer among individuals aged 15–19 years.[1] Gonadal toxicity from chemo-radiotherapy treatments can substantially impact male and female fertility.[2] In particular, young female cancer survivors commonly experience premature ovarian failure as one of the most significant

Importance of the Study

This study reviews the range of fertility preservation methods recommended by NICE as part of neuro-oncology patients' treatment. It highlights that among neuro-oncology patients, discussions of infertility risk are often lacking and therefore, only a minority of patients are currently undertaking fertility preservation. It demonstrates that neuro-oncology patients are safely able to undertake fertility preservation techniques as part of their treatment and can have good outcomes from this. To our knowledge, this is the first systemic review describing the use of fertility preservation techniques in neuro-oncology patients and their outcomes. It highlights the need for further high-quality studies to be produced before robust conclusions can be drawn.

long-term consequences.[3] With remarkable advancements in chemo-radiotherapy and surgical interventions, the overall survival rates for CNS cancers have substantially improved. Consequently, there is an escalating awareness of the profound impact these treatments have on the quality of life of cancer survivors.[1]

Various factors associated with CNS cancers can significantly affect patients' fertility. Tumor infiltration, radiotherapy, and cranial surgery can induce considerable damage to the hypothalamic–pituitary axis, though, hormone replacement can minimize the effects of this. Furthermore, the application of chemo-radiotherapy regimens can exert gonadotoxic effects, leading to premature ovarian insufficiency and impaired fertility.[4,5] Spinal irradiation may also render the endometrium unresponsive to hormonal therapy and increase the risk of miscarriage and premature delivery.[6] Recognizing the clinical significance of preserving future reproductive potential, the National Institute for Health and Care Excellence (NICE) has emphasized the importance of implementing fertility preservation techniques for individuals seeking to safeguard their fertility.[7]

A variety of methods exist for women who wish to safeguard their future reproductive potential, with many only recently transitioning from experimental to established practices. In females, the most recognized technique in fertility preservation is embryo cryopreservation.[8] However, recent advancements have positioned oocyte cryopreservation as a viable alternative for those without a partner. Both embryo and mature oocyte cryopreservation necessitate ovarian hyperstimulation to stimulate the growth of multiple follicles.[9] Following retrieval, mature oocytes or embryos, procured via in vitro fertilization, are cryopreserved and stored under ideal conditions for future use by the patients.[10] Medulloblastoma is one of the most prevalent types of brain tumors among children, especially among prepubertal girls and ovarian tissue cryopreservation has been studied as the most preferred type of fertility preservation.[11] This method involves transplanting frozen-thawed ovarian tissue into the pelvic cavity post-CNS tumor treatment. Despite being an emerging technique, successful outcomes have been reported in the literature with transplantation restoring ovarian activity in 95–95% of participants[12–14] and approximately 1 in 4 women giving birth to a healthy child.[15] However, concerns about tumor reseeding persist,[16] although the risk appears to be minimized in patients in complete remission.[15] For pre or post pubertal patients undergoing radiotherapy, ovarian transposition, or oophoropexy, can be employed as a fertility preservation strategy. This surgical procedure relocates the ovaries outside the radiation field, thereby reducing radiation-induced damage.[17] For pubertal and postpubertal males, sperm cryopreservation is a well-established and effective technique for fertility preservation.[18] In prepubertal males, methods such as gonadal shielding and experimental techniques including testicular tissue cryopreservation are gaining interest.[19] Increasing numbers of young adults with CNS cancers view future family planning as feasible. However, oncologists may exhibit reluctance in referring patients to reproductive specialists, despite societal support and patient interest. This hesitation may stem from concerns about conveying conflicting prognostic messages, discomfort in discussing fertility or sexuality, and a lack of knowledge or time.[18] This systematic review aims to collate and present the existing evidence on fertility preservation techniques in patients with CNS cancers.

Methods

Information Sources

This systematic review is reported in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement.[20] The protocol has been prospectively registered on PROSPERO (CRD42022352810) and published.[21] Pubmed, Embase, Medline, Cochrane, and Google Scholar were searched until April 2023 using search terms related to fertility preservation techniques in neuro-oncology patients. Non-English studies, editorials, animal studies, and guidelines were excluded.

Study Selection

Two reviewers (B.O. and J.S.) participated in the literature selection using the search terms previously published.[21] The references from all included studies and all included studies were manually reviewed for relevant articles.

Titles and abstracts of potential studies for inclusion underwent eligibility screening, with full texts procured for further evaluation. Two investigators reviewed each article for suitability. Any disagreements were settled following an independent review by a third reviewer. In

instances where multiple publications originated from a single cohort, only the publication with the largest sample size was included to prevent possible duplicate reporting. All full-text studies reporting at least 1 fertility preservation technique in neuro-oncology patients were included. Papers that did not report a fertility preservation technique, did not report outcomes specifically for neuro-oncology patients or were animal or cadaveric studies were excluded.

The following data was extracted from each study: a total number of participants, sex, age, tumor histology, treatment regimen, the radiation dose to ovaries (grays), the radiation dose to HPA (grays), type of fertility preservation, age at fertility preservation, follow up time, rate of success of fertility preservation, rate of pregnancy, oocyte numbers retrieved, rates of sperm cryopreservation, rate of return to rewarm, MII oocyte numbers retrieved/vitrified, and neonatal outcomes where available. Where data is missing, the authors will be consulted for further completing data.

The primary outcome was the success rate of the fertility preservation technique. This was defined as successful cryopreservation of oocytes, embryo, sperm or ovarian tissue, or successful surgical transposition.

Quality of Included Studies

The 2 reviewers independently evaluated study quality using the NIH (National Heart, Lung, and Blood Institute) risk-of-bias tool for any type of study. The 2 reviewers rated each domain of the included studies as having a low, high or unclear risk of bias. These ratings were then used to provide an overall quality score for the methodology of the article. Discrepancies between the 2 reviewers were resolved through discussion with a third reviewer to achieve a consensus.

Synthesis of Results and Risk of Bias

Statistical analysis was performed using R version 1.3.959 (R Foundation). Pooling calculations were performed using the Hedges–Vevea[22] random effects model if 2 or more studies reported the same outcome. Q statistics and I^2 index were used to test for heterogeneity with a 2-sided P value < .001 and $I^2 > 50\%$ indicating heterogeneity respectively. Publication bias was assessed using the Egger regression test and Begg and Mazumdar rank correlation if the effect size was 3 or more in the included studies. A 2-sided P value < .05 was considered significant.

Results

Study Selection

The search of the 5 databases elicited 47 results after the removal of duplicates. Sixteen articles assessing the use of fertility preservation techniques in neuro-oncology patients were included in the study. Studies where participants were not referred for or did not undergo fertility preservation were excluded (Figure 1).

Study Characteristics

The sixteen studies contained data from 237 participants, of whom 110 underwent fertility preservation. Ten studies described oocyte or embryo cryopreservation, 5 studies described ovarian tissue cryopreservation, 3 studies described laparoscopic oophorexy, wedge resection, or transposition of the ovary, and 3 studies described sperm cryopreservation. The publication date ranged between 2011 and 2021. Mean follow-up was 46.8 ± 30.4 months (min: 11 months, max: 77 months) with duration not reported in 12 studies. Five studies were prospective and 11 studies were retrospective. All studies were published in English. The characteristics of the included studies and the demographics of participants are elaborated in Table 1.

Quality Assessment

All studies included in the systematic review were of fair or good quality according to the NIH scoring tool. Suboptimal scores were present in 5 domains. Every study failed to provide a sample size justification or power description, or variance and effect estimates and none of the case series were consecutive (Tables 2–4).

Reproductive and Pregnancy Outcomes

Two studies assessed fertility preservation referral practices among oncologists and neurosurgeons. Of 128 patients included in the studies, on average, 62.5% of patients with a brain tumor accepted a referral to a fertility preservation specialist. Bradford et al. reported that only 32.8% of patients seen in the clinic had a documented risk of infertility and ultimately, 21% of patients underwent fertility preservation.

Thirteen studies reported the number of patients who successfully underwent fertility preservation. All 97 patients included in the studies successfully underwent fertility preservation. There was only 1 significant complication, aspiration pneumonia, that was successfully treated with a course of antibiotics recorded in the studies.

Two studies reported the number of patients who returned to rewarm or use their cryopreserved embryos, oocytes, tissue, or sperm. Of the 35 patients who underwent fertility preservation in these studies, only 1 (2.9%) returned to rewarm. On pooled analysis of the 2 studies, the pooled proportion of participants who returned to rewarm was 2.8% (95% CI [0.0027–0.23]; Figure 2). No significant heterogeneity was found in the pooling calculation (Q test $P = 1.0$ and $I^2 < 50\%$). Publication bias assessment could not be assessed due to insufficient sample size.

Four studies reported the number of healthy children conceived to patients using fertility preservation techniques. Of the 84 patients who underwent a fertility

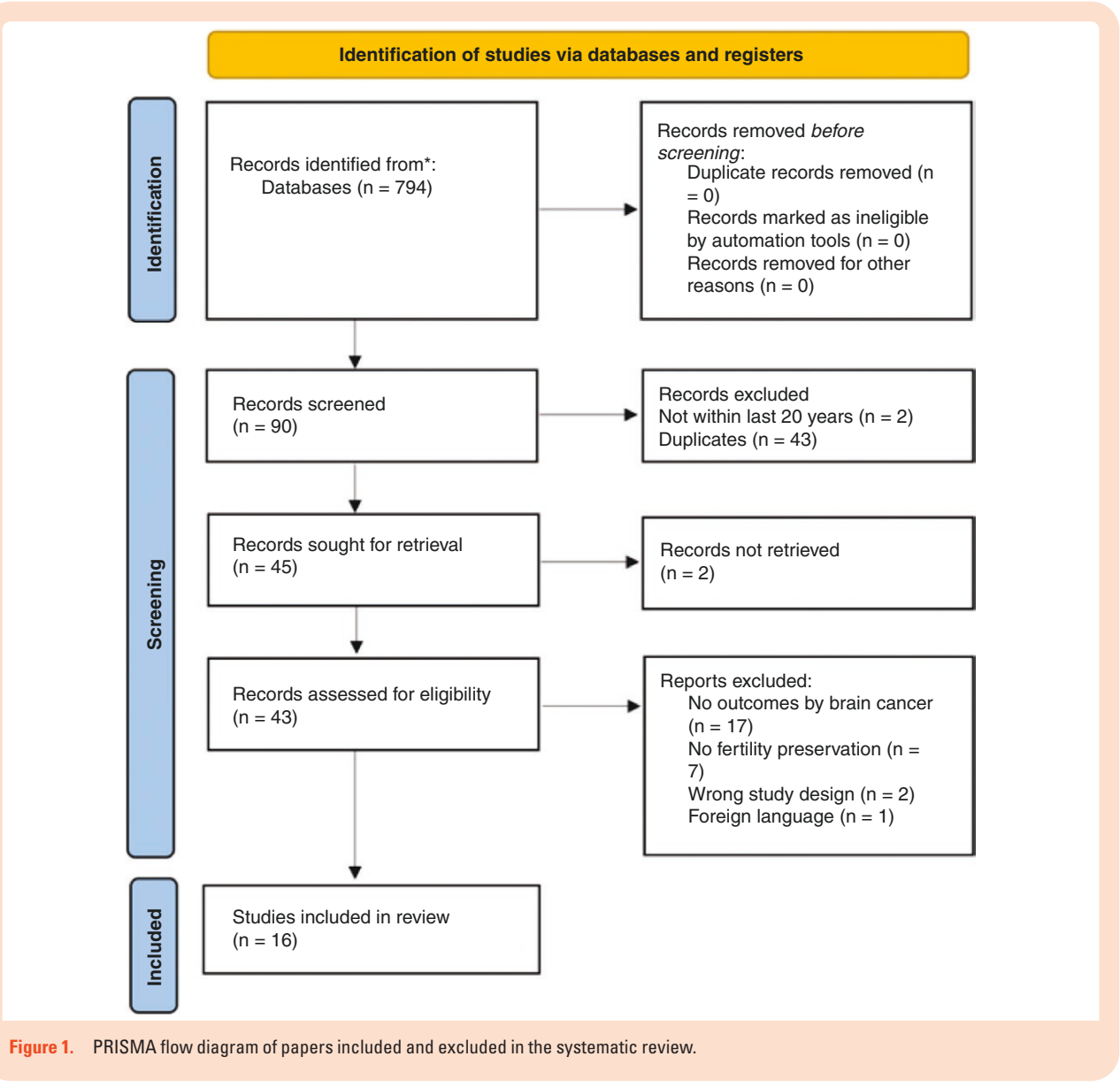

Figure 1. PRISMA flow diagram of papers included and excluded in the systematic review.

preservation technique, 5 (6.0%) patients successfully conceived 9 healthy children at term utilizing their cryopreserved sperm, embryos, or oocytes. Moreover, 6 patients successfully conceived naturally or using intrauterine insemination, resulting in 7 healthy-term children. On pooled analysis of the 4 studies that reported the number of live births, the proportion of live births following fertility preservation was 12% (95% CI [0.019–0.050]; Figure 3). There was significant heterogeneity ($I^2 > 50\%$, Q test $P = .24$) and publication bias (Eggers: $P = .01$ and Begg: $P = .04$) present in the pooling calculation.

Oocyte cryopreservation.—The number of oocytes retrieved from oocyte cryopreservation was recorded in 5 studies. On the pooling of the studies, there was a mean of 17.8 oocytes retrieved (95% CI [9.7–26.0]; Figure 4). There was significant heterogeneity ($I^2 > 50\%$ and Q P value = .04) or publication bias (Eggers: $P = .58$ and Begg: $P = .60$) found in the pooling calculation.

Discussion

Cancer has been identified as a prevalent indication for fertility preservation.[39] Recent advancements in cancer treatments and an emerging trend towards improved quality of life have led to increased consideration of fertility preservation (FP) techniques as part of patients' treatment.[1] This systematic review evaluated the best available evidence regarding FP techniques for patients with CNS tumors. Studies reported a range of fertility preservation techniques including oocyte cryopreservation, ovarian tissue cryopreservation, laparoscopic oophrophexy, and embryo cryopreservation. This study found that all patients

Table 1. Characteristics and Demographics of Included Studies

Study	Country	Study Design	Population (*n*)	Age	Female (%)	Cancer Diagnosis	Follow Up (months)	FP Technique
Abir et al., 2016[23]	Israel	Retrospective cohort study	5	5.8 ± 4.4	100	1 × brain ATRT, 2 × medulloblastoma,1 × brain PNET, 1 × neuroblastoma	NA	OC, OTC
Armstrong et al., 2018[24]	USA	Retrospective cohort study	12	7.5 ± 4.0	100	1 × optic pathway pilocytic astrocytoma, 1 × pineoblastoma, 1 × medulloblastoma, 1 × brain PNET (metastatic), 8 × neuroblastoma	NA	OTC
Bradford et al., 2018[25]	Australia	Retrospective cohort study	58	NA	NA	NA	NA	SC, OC, EC, ST
Creux et al., 2017[26]	Canada	Retrospective cohort study	25	26.4 ± 5.0	100	NA	NA	OC
Das et al., 2011[27]	Canada	Retrospective case–control study	5	29.4 ± 0.8	100	Astrocytoma and high-grade glioma	NA	OC, EC
Kasei et al., 2020[28]	Japan	Retrospective case report	3	2.0 ± 1.0	100	1 × yolk-sac tumor in sacral region, 1 × retroperitoneal neuroblastoma, and 1 × cerebellar medulloblastoma	NA	OTC
Kim et al., 2016[29]	USA	Prospective cohort study	12	NA	100	NA	NA	OC, EC
Kung et al., 2008[30]	Taiwan	Prospective case series	5	14.4 ± 2.7	100	3 × germinoma and 2 × medulloblastoma	66 ± 46	ST
Kutteh et al., 2018[31]	USA	Prospective case series	3	14.6 ± 1.0	100	3 × medulloblastoma	NA	OC
Lester-Coll et al., 2014[32]	USA	Prospective case report	1	18	100	1 × disseminated germinoma	11	ST
Nguyen et al., 2021[33]	Belgium	Prospective cohort study	20	10.5 ± 7.2	100	8 × medulloblastoma, 3 × ependymoma, 3 × PNET, 2 × astrocytoma, 2 × glioblastoma, and 2 × CNS germinoma	NA	OTC
Nguyen et al., 2020[34]	Belgium	Retrospective case series	3	10 ± 6.6	100	3 × PNET	77 ± 68	OTC
Nordan et al., 2020[35]	USA	Retrospective case–control study	10	30.4 ± 4.5	100	10 × glioma	NA	OC, EC
Nurudeen et al., 2016[36]	USA	Retrospective cohort study	4	NA	100	NA	NA	OC, EC
Peyser et al., 2018[37]	USA	Retrospective case report	1	33	100	1 × anaplastic astrocytoma	33	OC
Stone et al., 2017[38]	USA	Retrospective Cross-sectional study	70	32	45.7	62 × glioma, 16 × oligodendroglioma, 3 × ependymoma, 2 × CNS lymphoma, 2 × other/unknown, and 1 × meningioma	NA	SC, OC, EC

FP, Fertility preservation; all presented as mean ± SD unless stated otherwise.

successfully underwent fertility preservation with minimal complications. It demonstrated that neuro-oncology patients were able to successfully conceive healthy children utilizing fertility preservation techniques.

Despite increasing societal demand, this study observed a significant gap in fertility preservation discussions before treatment. NICE recognizes the importance of fertility preservation discussions in the oncology setting,[7] given that both cancer and treatments such as radiotherapy and chemotherapy can have an impact on fertility status.[40] However, only 32.8% of patients reviewed in the clinic had a documented discussion of infertility, highlighting the crucial need for increased awareness of fertility preservation techniques amongst both physicians and patients. This reflects findings described by Daly et al. who found a large proportion of brain tumor patients were not informed of the impact on fertility due to practitioners' concern regarding poor prognosis.[41] This may be due to the high proportion of females included in the studies in the systematic review. Male patients have traditionally had more awareness regarding fertility preservation techniques as sperm banking is a less invasive, less expensive, and

Table 2. Quality Assessment of Included Studies: Cohort and Cross-Sectional Studies

Author	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)	(12)	(13)	(14)	Rating
Abir et al.[23]	1	1	NA	1	0	1	0	1	1	1	1	0	NA	0	Fair
Armstrong et al.[24]	1	1	1	1	0	1	0	1	1	1	1	1	NA	1	Good
Bradford et al.[25]	1	1	1	1	0	1	NA	1	1	1	1	0	NA	1	Good
Creux et al.[26]	1	1	1	1	0	1	0	1	1	1	1	0	NA	1	Good
Kim et al.[29]	1	1	1	1	0	1	0	1	1	1	1	0	NA	1	Good
Nguyen et al.[34]	1	1	1	1	0	1	NA	1	1	1	1	0	NA	1	Good
Nurudeen et al.[36]	1	1	1	1	0	1	NA	1	1	1	1	NA	NA	1	Good
Stone et al.[38]	1	1	1	1	0	1	NA	1	1	1	1	0	NA	1	Good

(1) Was the research question or objective in this paper clearly stated? (2) Was the study population clearly specified and defined? (3) Was the participation rate of eligible persons at least 50%? (4) Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were inclusion and exclusion criteria for being in the study prespecified and applied uniformly to all participants? (5) Was a sample size justification, power description, or variance and effect estimates provided? (6) For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured? (7) Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed? (8) For exposures that can vary in amount or level, did the study examine different levels of the exposure as related to the outcome (eg categories of exposure, or exposure measured as a continuous variable)? (9) Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants? (10) Was the exposure(s) assessed more than once over time? (11) Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants? (12) Were the outcome assessors blinded to the exposure status of participants? (13) Was the loss to follow-up after baseline 20% or less? (14) Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s)?

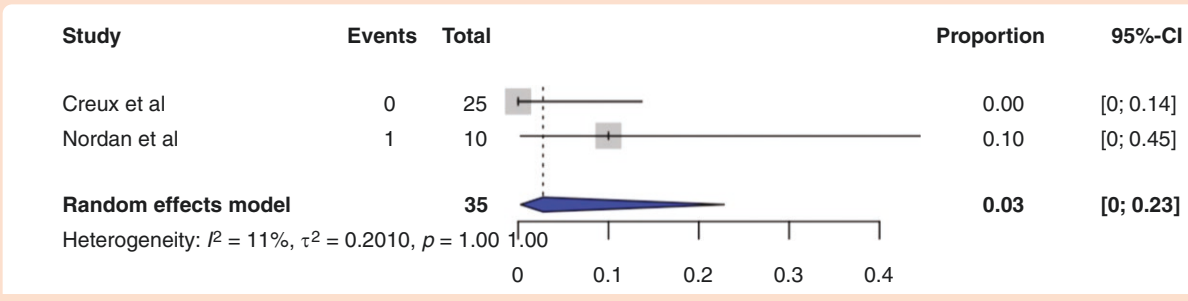

Figure 2. Forest plot of the proportion of participants who returned to rewarm.

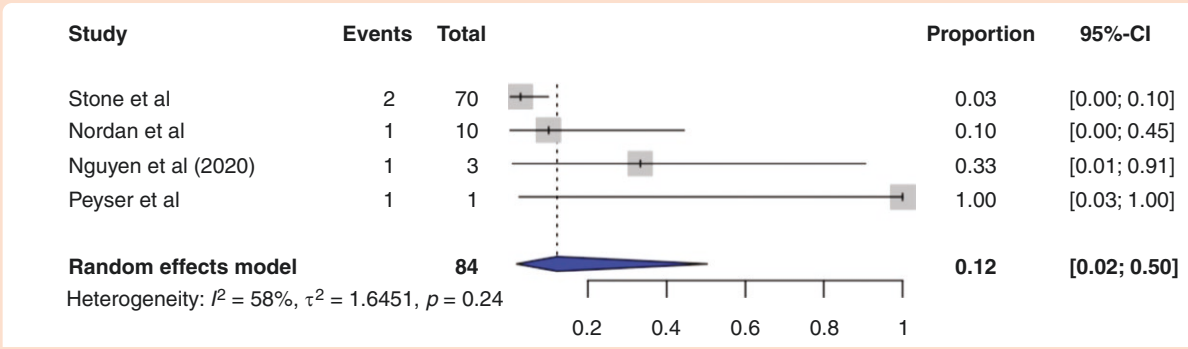

Figure 3. Forest plot of the proportion of participants who delivered healthy children using fertility preservation.

more established technique.[38,42] Furthermore, this study demonstrated a high acceptance rate (62.5%) for fertility preservation techniques in neuro-oncology patients. There are many factors that can influence the choice of fertility preservation techniques, from patients' priorities to marital status. Specifically, patients without children are more

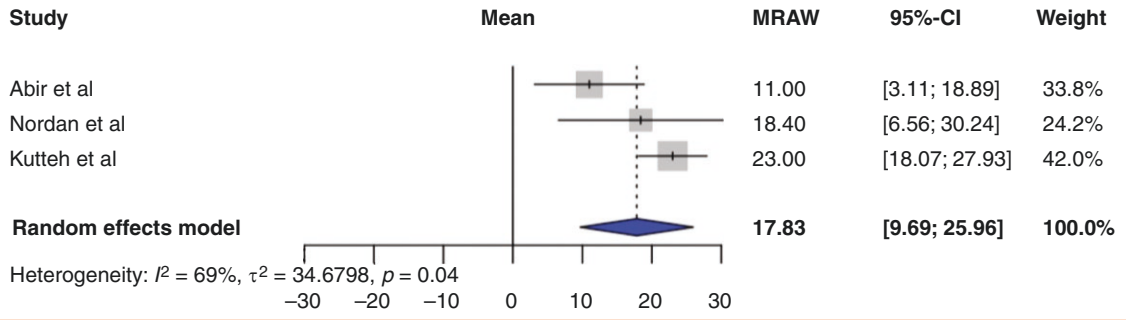

Figure 4. Forest of the pooled mean of oocytes retrieved through oocyte cryopreservation Of the oocytes retrieved, on pooled calculation 78% (95% CI [67–86%); Figure 5) were successfully frozen. There was no significant heterogeneity in the pooling calculation (I^2 < 50% and Q P value = .97). There was publication bias identified in the calculation (Eggers: P = .11 and Begg: P = .04).

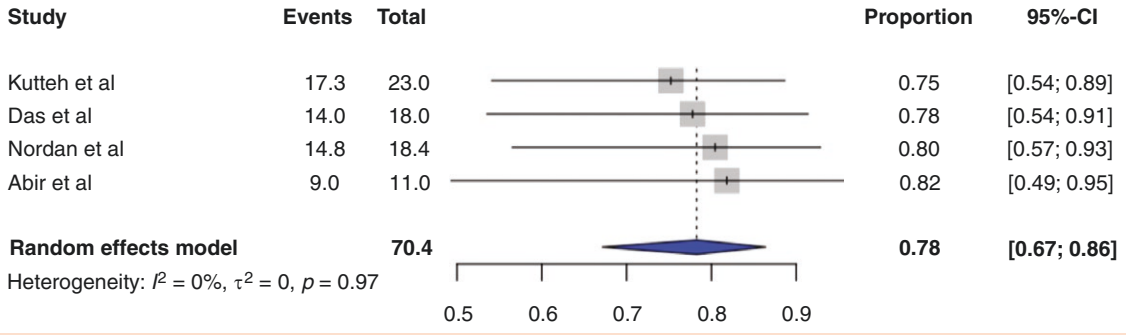

Figure 5. Forest plot of the proportion of oocytes frozen from those retrieved by fertility preservation.

Table 3. Quality Assessment of Included Studies: Case–Control Studies

Author	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)	(12)	Rating
Das et al.[27]	1	1	0	1	1	1	NA	1	1	1	0	0	Fair
Nordan et al.[35]	1	1	0	1	1	1	NA	1	1	1	0	1	Good

(1) Was the research question or objective in this paper clearly stated and appropriate? (2) Was the study population clearly specified and defined? (3) Did the authors include a sample size justification? (4) Were controls selected or recruited from the same or similar population that gave rise to the cases (including the same timeframe)? (5) Were the definitions, inclusion and exclusion criteria, algorithms or processes used to identify or select cases, and controls valid, reliable, and implemented consistently across all study participants? (6) Were the cases clearly defined and differentiated from controls? (7) If less than 100 percent of eligible cases and/or controls were selected for the study, were the cases and/or controls randomly selected from those eligible? (8) Was there use of concurrent controls? (9) Were the investigators able to confirm that the exposure/risk occurred prior to the development of the condition or event that defined a participant as a case? (10) Were the measures of exposure/risk clearly defined, valid, reliable, and implemented consistently (including the same time period) across all study participants? (11) Were the assessors of exposure/risk blinded to the case or control status of participants? (12) Were key potential confounding variables measured and adjusted statistically in the analyses? If matching was used, did the investigators account for matching during the study analysis?

likely to accept referrals for fertility preservation techniques compared to those with children.[38] Central nervous system tumors are the most prevalent cancer in patients aged 15–19, who are unlikely to have children at the time of diagnosis.[1] Moreover, previous studies have suggested that young patients may not consider the impact of cancer and its treatments on fertility as seriously as older counterparts.[43] This highlights the importance of promoting fertility preservation techniques amongst neuro-oncology patients and given the young age of this cohort, that parents or guardians are fully informed on the potential effects of cancer and potential therapies on fertility.

Choosing the most appropriate fertility preservation technique for the individual patient is essential. Many factors may contribute to this, including, patient choice, partner status, and pubertal status. Patients who are older, have a lower pretreatment anti-Müllerian hormone and are undergoing more aggressive anticancer treatments are at

Table 4. Quality Assessment of Included Studies: Case Series

Author	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	Rating
Kasei et al.[28]	1	1	0	1	1	1	1	NA	1	Good
Kung et al.[30]	1	1	0	1	1	1	1	NA	1	Good
Kutteh et al.[31]	0	1	0	1	1	1	1	NA	1	Fair
Nguyen et al.[33]	1	1	0	1	1	1	1	NA	1	Good

(1) Was the study question or objective clearly stated? (2) Was the study population clearly and fully described, including a case definition? (3) Were the cases consecutive? (4) Were the subjects comparable? (5) Was the intervention clearly described? (6) Were the outcome measures clearly defined, valid, reliable, and implemented consistently across all study participants? (7) Was the length of follow-up adequate? (8) Were the statistical methods well-described? (9) Were the results well-described?

increased risk of gonadotoxicity.[44] This study observed positive outcomes in patients undergoing fertility preservation techniques with 3% of patients returning to rewarm their embryos, and 12% of patients who underwent a fertility preservation technique successfully conceiving a healthy child at term. This is fairly consistent with previous publications which observed that 5.6% and 7.2% of their population returned to rewarm their frozen material.[45,46] The lower return to rewarm observed in this study may be due to the short follow-up period, high mortality rate and young average age of patients in the studies included. This study also noted that participants were able to conceive naturally. Stone et al. have highlighted this previously, with 3 in 5 men and some women being able to conceive naturally following treatment with surgical resection and focal radiotherapy.[38]

The most established technique in females is oocyte or embryo cryopreservation. A recent meta-analysis has demonstrated live birth rates of 41% following IVF and 32% using vitrified oocytes.[47] Previous studies have observed a similar mean number of oocytes retrieved, proportion of oocytes retrieved and oocyte fertilization rates between cancer patients and controls[48–50] In fact, it is believed that there is a similar live birth rate per transfer of embryos between patients undergoing embryo cryopreservation for cancer compared to noncancer patients.[51] However, few outcomes are reported in studies assessing neuro-oncology patients and little is known about the fertility capabilities of prepubertal oocytes regarding their potential for fertilization or embryogenesis or the safety of their use if collected following chemotherapy. There is also little evidence regarding the possible interactions between gliomas and pregnancy. Tumor subtypes might undergo a biological behavior change during pregnancy including malignant transformation or accelerated growth.[52–55] Peyser et al. recommend follow-up with serial MRI in addition to obstetric monitoring in patients with glioma wishing to be pregnant.[37]

Studies assessing the success of ovarian tissue cryopreservation and transplantation have been positive. Jadoul et al. demonstrated a 33% success rate through ovarian auto transplantation.[56] They reported a 96% satisfaction rate amongst those undergoing ovarian tissue cryopreservation and a low rate of complications. However, there is still much uncertainty surrounding this technique. There are no guidelines as to how much ovarian tissue should be retrieved, particularly in prepubertal patients and there are ongoing concerns regarding malignant reseeding in the transplanted ovarian tissue.[57,58] In fact, the risk of ovarian metastases cannot be completely ruled out due to the lack of specific detection methods and the possibility of sampling error.[59]

Limitations Paragraph

To our knowledge, this is the first systematic review describing the use of fertility preservation techniques in neuro-oncology patients and their outcomes. The main limitation of the study is the paucity of data: only 16 studies were included in the systematic review with heterogenous outcomes reported, making pooling of the results difficult, and therefore, the conclusions that can be drawn from this paper, are limited. The quality of the studies is also a significant limitation, with most studies being case reports or case series. Furthermore, there was significant heterogeneity among the studies in terms of stimulation protocols, gonadotrophin doses, and timings of interventions. When combined with the lack of randomized control trials included in the study, this may confound results. This study lacked the data to compare the outcomes between fertility preservation techniques and robust conclusions are difficult to draw due to a lack of control group. It is evident that there is significant variability in the quality and content of guidelines making recommendations for fertility preservation in cancer patients. Further high-quality studies are required before reliable conclusions can be drawn.

Conclusions

This study highlights the importance of personalized fertility preservation counseling in neuro-oncology patients. It is essential patients are provided with a detailed discussion on the possible implications of pathology on future fertility and that physicians have the confidence to consider a referral to a fertility specialist. However, it is evident that further studies concerning the risks, benefits, long-term outcomes, and cost-effectiveness of these techniques are required.

Keywords

embryo cryopreservation | fertility preservation | neuro-oncology | oocyte cryopreservation | ovarian tissue transposition

Funding

The authors declare that no funds, grants, or other support were received during the preparation of this manuscript.

Conflict of interest statement

The authors have no relevant financial or nonfinancial interests to disclose.

Authorship statement

All authors contributed to the study's conception and design. Material preparation, data collection, and analysis were performed by M.O.-G., O.C.B., and J.K.S. The first draft of the manuscript was written by M.O.-G. and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Ethics approval

Ethics approval was not required due to this being a systematic review.

Data availability

Data is available on request.

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