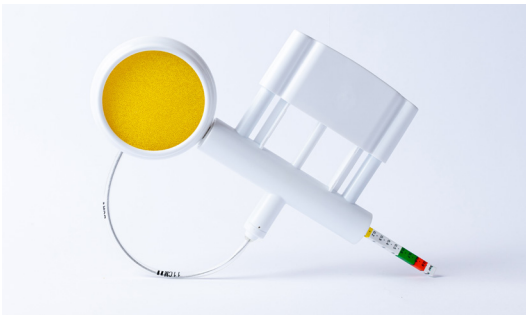
research

Chemotherapy in nasopharyngeal carcinoma
p 395



Risk of sphincter injury after vacuum delivery
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ORIGINAL RESEARCH Randomised phase 3 clinical trial

Nab-paclitaxel, cisplatin, and capecitabine versus cisplatin and gemcitabine as first line chemotherapy in patients with recurrent or metastatic nasopharyngeal carcinoma

Liu GY, Ye YF, Jiang YF, et al

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Study question How do the efficacy and safety of nab-paclitaxel, cisplatin, and capecitabine (nab-TPC) compare with those of gemcitabine plus cisplatin as first line chemotherapy in patients with recurrent or metastatic nasopharyngeal carcinoma.

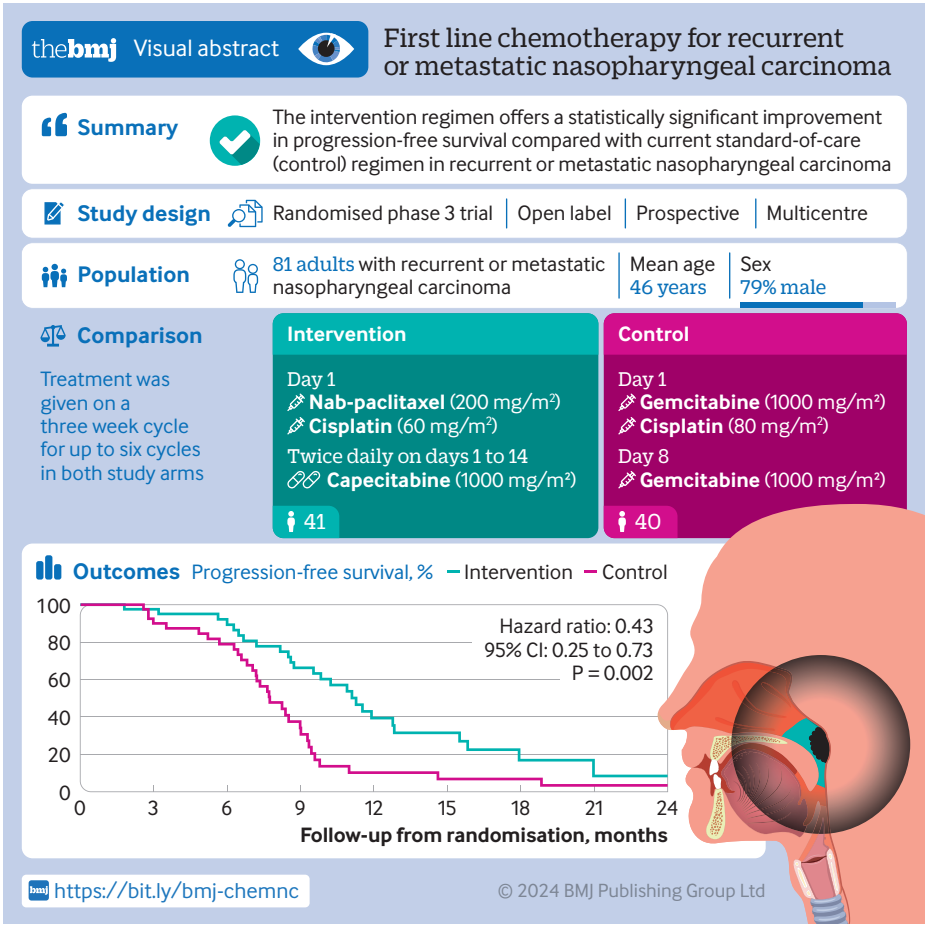
Methods This multicentre, randomised, phase 3 trial enrolled 81 adults (≥18 years) with untreated recurrent or metastatic nasopharyngeal carcinoma in four hospitals in China between September 2019 and August 2022. Patients were randomly assigned in a 1:1 ratio to receive either nab-TPC (nab-paclitaxel 200 g/m^2 on day 1, cisplatin 60 mg/m^2 on day 1, and capecitabine 1000 mg/m^2 twice on days 1-14) or gemcitabine plus cisplatin (gemcitabine 1000 mg/m^2 on days 1 and 8 and cisplatin 80 mg/m^2 on day 1). Progression-free survival was evaluated by the independent review committee as the primary endpoint in the intention-to-treat population.

Study answer and limitations The median progression-free survival was 11.3 (95% confidence interval (CI) 9.7 to 12.9) months in the nab-TPC cohort versus 7.7 (6.5 to 9.0) months in the gemcitabine plus cisplatin cohort. The hazard ratio was 0.43 (95% CI 0.25 to 0.73; P=0.002). The objective response rate in the nab-TPC cohort was 83% (34/41) versus 63% (25/40) in the gemcitabine and cisplatin cohort (P=0.05), and the duration of response was 10.8 months in the nab-TPC cohort compared with 6.9 months in the gemcitabine and cisplatin cohort (P=0.009). Longer follow-up is needed to confirm the overall survival benefit. Whether the findings can be extrapolated to non-endemic regions without further validation remains uncertain as participants were sourced from endemic areas in China where non-keratinising nasopharyngeal carcinoma comprises more than 95% of cases.

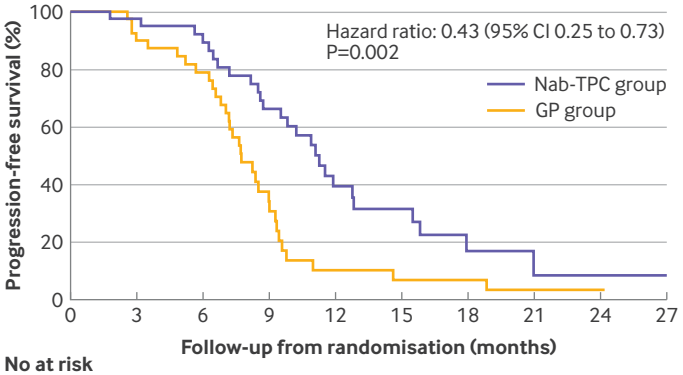
What this study adds The findings show that the nab-TPC regimen offers a statistically significant improvement in progression-free survival compared with the current standard of care gemcitabine plus cisplatin regimen in recurrent or metastatic nasopharyngeal carcinoma.

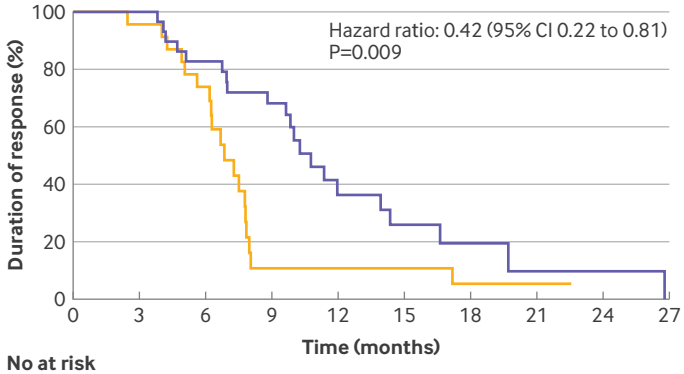
Funding, competing interests, and data sharing This study was mainly supported by the Guangdong Basic and Applied Basic Research Foundation, the National Natural Science Foundation of China, China Postdoctoral Science Foundation (CPSF), and Postdoctoral Fellowship Program of CPSF. No competing interests declared. Researchers interested in using the raw data for scientific research purposes may request access via the corresponding authors.

Study registration Chinese Clinical Trial Registry ChiCTR1900027112.



Longer follow-up is needed to confirm the overall survival benefit





No at risk

Nab-TPC group	41	39	32	23	11	7	3	1	1
GP group	40	35	28	10	3	2	2	1	1

No at risk

Nab-TPC group	34	30	24	18	8	5	2	1	1
GP group	25	22	16	2	2	2	1	1	0

Kaplan-Meier plots of progression-free survival (left) and duration of response (right) assessed by independent image review from randomly assigned patients. CI=confidence interval; GP=gemcitabine and cisplatin; Nab-TPC=nab-paclitaxel, cisplatin, and capecitabine

Lateral episiotomy during vacuum assisted childbirth

ORIGINAL RESEARCH Multicentre, open label, randomised controlled trial

Lateral episiotomy or no episiotomy in vacuum assisted delivery in nulliparous women (EVA)

Bergendahl S, Jonsson M, Hesselman S, et al

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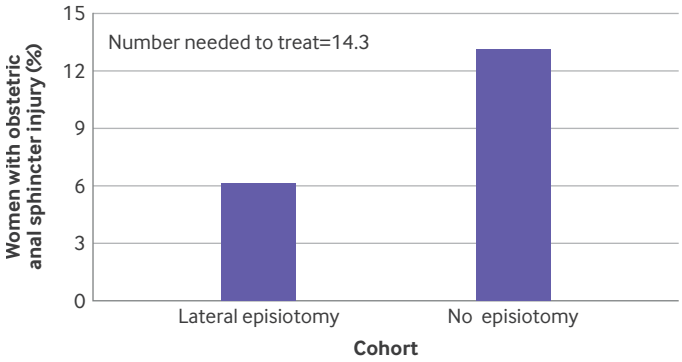
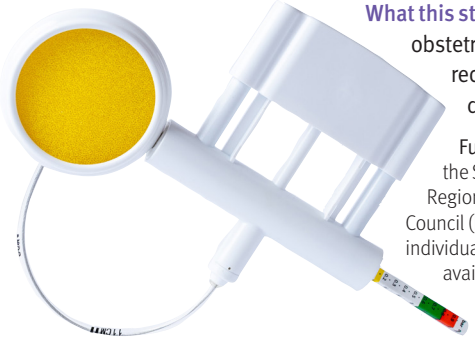
Study question Can routine lateral episiotomy prevent obstetric anal sphincter injury in nulliparous women requiring vacuum assisted delivery?

Methods The Episiotomy in Vacuum Assisted delivery (EVA) study was a multicentre, open label, randomised controlled trial that investigated the effect of lateral episiotomy on obstetric anal sphincter injury in 702 nulliparous women. Women were eligible if they gave birth at one of eight hospitals in Sweden between 1 July 2017 and 15 February 2023 to a singleton live baby of 34 gestational weeks or older with vacuum assisted delivery. Participants were randomly assigned to either routine lateral episiotomy or to no episiotomy at the time of fetal head crowning. Primary analyses were in the modified intention to treat population. The number needed to treat was calculated.

Study answer and limitations Obstetric anal sphincter injury in nulliparous women requiring vacuum assisted delivery was more than halved among those in the lateral episiotomy group (21 (6%) of 344 women) compared with women in the no episiotomy group (47 (13%) of 358 women) (P=0.002). The risk difference was −7.0% (96% confidence interval (CI) −11.7% to −2.5%). The risk ratio adjusted for study site was 0.47 (96% CI 0.23 to 0.97) and unadjusted was 0.46 (0.28 to 0.78). The number needed to treat with episiotomy was 14.3 (96% CI 8.6 to 40.0) to avoid one obstetric anal sphincter injury. No clear difference was noted between the groups regarding blood loss, perineal pain post partum, birth experience, or neonatal outcomes. Women who were assigned to the episiotomy group had more wound complications than those in the no episiotomy group. The main limitation was that the trial was not blinded, but this design was deemed not feasible because an episiotomy would have been apparent.



Proportion of obstetric anal sphincter injury in women allocated to lateral episiotomy and to no episiotomy



What this study adds Routine lateral episiotomy led to fewer obstetric anal sphincter injuries in nulliparous women requiring vacuum assisted delivery than women who did not have a lateral episiotomy.

Funding, competing interests, and data sharing Funded by the Swedish Research Council (2016-00526), the Stockholm Region (FoUI-960261/2021), and the Uppsala-Örebro Research Council (RFR-939428). No competing interests declared. Deidentified individual participant data and a data dictionary may be made available on request.

Study registration ClinicalTrials.gov NCT02643108.

Bergendahl and colleagues' study provides much needed evidence supporting the use of episiotomy to prevent obstetric anal sphincter injury among nulliparous women needing vacuum assisted birth.[1] The authors should be commended for conducting a well designed randomised trial with short and long term outcomes, which concluded that lateral episiotomy can be recommended for nulliparous women requiring vacuum extraction substantially to reduce the rate of obstetric anal sphincter injuries.

What does reducing anal sphincter injuries by more than half mean to birthing women? Although all forms of perineal injury cause morbidity, injury to the anal sphincter is associated with worse perineal pain, dyspareunia, and sexual dysfunction.[2 3] Anal sphincter injury is also a major risk factor for anal incontinence, with about 38% of affected women developing symptoms after primary repair.[4]

Anal sphincter injuries can have a devastating and life changing impact on women and their families; the emotional trauma and psychological symptoms can have a similar or even more substantial effect than the physical symptoms.[5] Patients may be unable to return to their previous work, and some are unable to work at all.[6]

The management of perineal trauma and its sequelae contribute substantially to healthcare costs. In 2013 and 2014, the economic burden of obstetric anal sphincter injuries in the UK ranged between £3.7m (€4.4m; $4.7m) (with assisted vaginal birth) and £9.8m (with spontaneous vaginal birth).[7] In the US, complications associated with perineal trauma cost about $83m between 2007 and 2011.[8] Given the scale of morbidity and associated costs, measures to minimise anal sphincter injury during childbirth should be prioritised by health leaders, clinicians, and policy makers. This involves identifying and reducing modifiable risk factors, such as an episiotomy with vacuum assisted births.

Prevention is complex, however, as causes are multifactorial. Evidence based strategies include antenatal perineal massage, use of warm compresses and perineal massage during the second stage of labour,[9] manual protection of the perineum,[10] performing an episiotomy when indicated at an angle of 60° from the midline,[11] and choosing vacuum assistance over forceps if clinically indicated.[12 13] A growing body of evidence from several countries, including the UK, Norway, and Denmark, shows that perineal protection initiatives and care bundles can reduce the incidence of anal sphincter injuries during childbirth.[10-15] In the UK, the Royal College of Obstetricians and Gynaecologists and the Royal College of Midwives recommend a care bundle associated with a 20% reduction in these injuries.[16]

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Anal sphincter injuries can have a devastating and life changing impact on women and their families

Variability of injury rates

Although Bergendahl and colleagues' new trial shows that use of episiotomy during vacuum assisted birth significantly reduces the risk of an anal sphincter injury, practices during childbirth are complex and influenced by both anecdote and the availability of trained staff. This may explain the wide variation in both episiotomy and anal sphincter injury rates among women having instrumental births in Europe, Canada, and the US.[17] Instrumental births using forceps remain prevalent in most of the English speaking countries, as well as in eastern Europe and South America; whereas vacuum assisted is most popular in Africa, Asia, and northern Europe.[18] Bergendahl and colleagues' trial provides compelling evidence of the benefit of episiotomy with vacuum assisted birth. A systematic review has shown that similar findings apply to forceps birth with the use of mediolateral episiotomy (incision beginning in the midline and directed laterally and downward) or lateral episiotomy, but adequately powered randomised studies are lacking.[19]

Mediolateral episiotomy is the most frequently used type of episiotomy in Europe.[20] Can the findings of the study by Bergendahl and colleagues be extrapolated to a mediolateral episiotomy? Yes—obstetric anal sphincter injury with lateral episiotomy (incision begins in the vaginal introitus 1 or 2 cm lateral to the midline) has been shown not to differ significantly from a mediolateral episiotomy in terms of the incidence and extent of pain in the first 10 days.[21] However, it is essential to ensure that the cut is at an angle of 60° from the midline when the fetal head distends the perineum. Doctors and midwives need more training to maintain this angle, as the closer the cut is to the anal sphincter, the higher the risk of anal sphincter injury.[22] Further research is also needed to explore whether the favourable outcomes in the new trial can be replicated in populations with higher baseline rates of anal sphincter injury.

Predicting risk

In an ideal world, a prediction model would be developed to identify women at risk of obstetric anal sphincter injury to help provide personalised care,[23] possibly utilising machine learning.[24] In the meantime, comprehensive antenatal information and compassionate evidence based care after birth remain essential for all affected women and their partners. Education and training in how to reduce women's risk of anal sphincter injuries have improved in the UK after the inclusion of the perinatal pelvic health programme in the NHS long term plan.[25] The multidisciplinary approach of the Royal College of Obstetricians and Gynaecologists and Royal College of Midwives to developing care bundles has been an important step forward. However, there is much more to do.

The findings from Bergendahl and colleagues' trial will encourage more consistent counselling and clinical decision making during the antenatal period and during labour and delivery. Research should continue to help inform a global consensus on the prevention of perineal trauma within all maternity services.

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