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НАУЧНО-ПРАКТИЧЕСКИЙ МЕДИЦИНСКИЙ ЖУРНАЛ

META-ANALYSIS:
Cervical volume predicts labour induction success

ORIGINAL STUDY:
3D head model for Gasserian ganglion puncture training

CLINICAL CASE:
Acanthocytosis indicates poor outcomes in liver cirrhosis

Sechenov Medical Journal

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Цели и задачи: к основным целям журнала относятся представление актуальных научных достижений российских и зарубежных ученых в области медико-биологических наук, фундаментальной и клинической медицины, увеличение значимости и авторитета российской медицинской науки за счет повышения качества научных публикаций. Издание предназначено для профессионалов в области здравоохранения.

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Телефон редакции: +7 (926) 306-39-99
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CONTENT

СОДЕРЖАНИЕ

Review / Обзор
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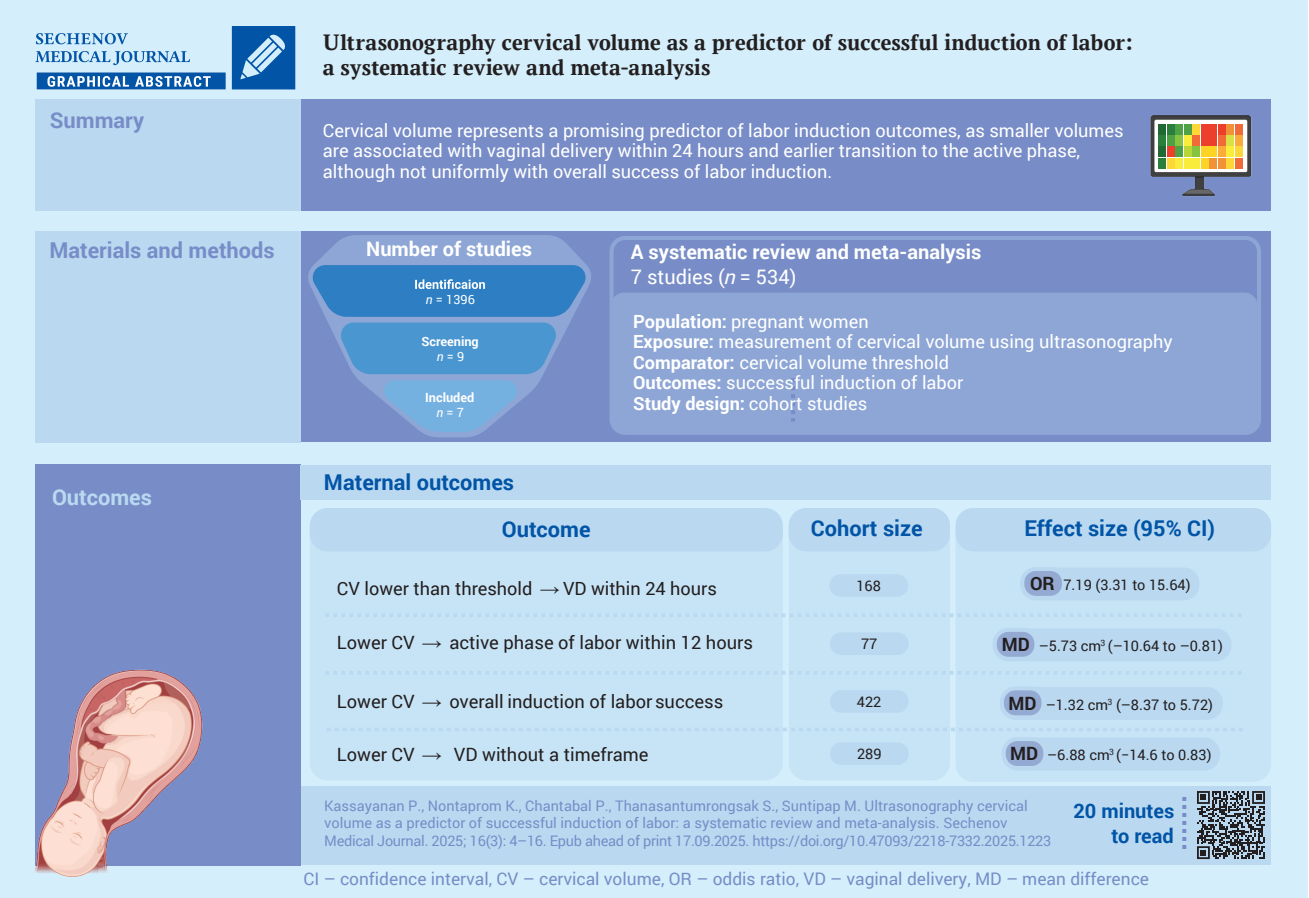
Ultrasonography cervical volume as a predictor of successful induction of labor: a systematic review and meta-analysis

Potsanop Kassayanan[1], Kasidis Nontaprom[1], Prame Chantabal[2], Switta Thanasantumrongsak[1], Monchai Suntipap[1,✉]
[1]Srinakharinwirot University
114, Sukhumvit 23 str., Wattana District, Bangkok, 10110, Thailand
[2]Khlong Luang Hospital
30, M.7 Khlong Hok, Khlong Luang District, Pathum Thani, 12120, Thailand



Abstract

Aim. To compare the cervical volume of patients who underwent successful and failed induction of labor (IOL) procedures.

Materials and methods. This systematic review and meta-analysis were conducted according to PRISMA guidelines. A comprehensive literature search was performed in PubMed, EMBASE, Scopus, and Google Scholar to identify cohort studies published between January 01, 2005 and December 31, 2024, that compared cervical volume in pregnant women who underwent IOL. A random-effects meta-analysis was performed.

Results. Seven studies involving 534 pregnant women were included. Four studies were considered low risk of bias and two studies were regarded as high risk of bias. Risk of bias assessment could not be performed in one study because the full-text of the article was not available. The pooled analysis of two studies involving 168 pregnant women demonstrated a positive association between the lower cervical volume and successful vaginal delivery within 24 hours (odds ratio 7.19; 95% confidence interval: 3.31 to 15.64; I^2 = 0%). The pooled analysis of five studies

involving 422 pregnant women showed no statistically significant difference between successful and failed IOL, with a mean difference −1.32 cm^3; 95% confidence interval: −8.37 to 5.72; I^2 = 89.8%). Subgroup analyses showed no statistically significant association between cervical volume and successful IOL when defined as vaginal delivery without time restriction or within 24 hours. However, a significantly lower cervical volume was observed in women who achieved the active phase of labor within 12 hours. The Egger's regression test confirmed the absence of small-study effects (coefficient = 0.50, standard error = 1.75, p = 0.78).
Conclusion. Cervical volume has significant potential as a parameter for predicting successful IOL, with a smaller cervical volume being associated with better outcomes, although subgroup findings remain inconsistent.

Keywords: cervical volume; ultrasound imaging; induced labour; vaginal delivery; cesarean delivery
MeSH terms:
LABOR, INDUCED – METHODS
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CONTACT INFORMATION:
Monchai Suntipap, MD, MSc, Doctor, lecturer, Department of Obstetrics and Gynecology, Srinakharinwirot University.
Address: 114, Sukhumvit 23 str., Wattana District, Bangkok, 10110, Thailand
E-mail: monchai@g.swu.ac.th

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Объем шейки матки, оцененный по ультразвуковому исследованию, как предиктор успешной родовой деятельности: систематический обзор и метаанализ

П. Кассаянан[1], К. Нонтапром[1], П. Чантабал[2], С. Танасантумронгсак[1], М. Сунтипап[1,✉]
[1]Университет Сринакаринвирот
ул. Сукхумвит 23, д. 114, район Ваттана, г. Бангкок, 10110, Таиланд
[2]Больница Клонг Луанг
М.7 Клонг Хок, д. 30, район Клонг Луанг, г. Патхумтхани, 12120, Таиланд

Аннотация

Цель. Сравнить объем шейки матки у пациенток с успешной и неуспешной индукцией родовой деятельности (ИРД).
Материалы и методы. Систематический обзор и метаанализ выполнен в соответствии с рекомендациями PRISMA. Поиск литературы проводился в базах PubMed, EMBASE, Scopus и Google Scholar для выявления когортных исследований, опубликованных в период с 1 января 2005 по 31 декабря 2024 года, в которых сравнивался объем шейки матки у беременных женщин, перенесших ИРД. Для метаанализа использовали модель со случайными эффектами.

Результаты. В анализ включены семь исследований с участием 534 беременных женщин. В четырех исследованиях выявлен низкий риск систематических ошибок, в двух – высокий; в одном исследовании оценка риска не выполнена из-за отсутствия полного текста. При объединенном анализе двух исследований (n = 168) обнаружена положительная связь между меньшим объемом шейки матки и успешными естественными родами в течение 24 часов (отношение шансов 7,19; 95% доверительный интервал: 3,31–15,64; I^2 = 0%). При объединенном анализе пяти исследований (n = 422) не выявлено статистически значимой разницы между успешной и неуспешной ИРД (разница средних −1,32 см³; 95% доверительный интервал: −8,37–5,72; I^2 = 89,8%). Анализ подгрупп не выявил статистически значимой связи между объемом шейки матки и успешной ИРД при определении исхода как естественные роды без ограничения по времени или продолжительностью до 24 часов. Вместе с тем существенно меньший объем шейки матки отмечен у женщин, достигших активной фазы родов в срок до 12 часов. Тест Эггера подтвердил отсутствие публикационных смещений (коэффициент = 0,50; стандартная ошибка = 1,75; p = 0,78).
Заключение. Определение объема шейки матки в качестве параметра для прогнозирования успешной ИРД обладает значительным потенциалом; меньшие значения ассоциируются с лучшими исходами, хотя результаты анализа подгрупп остаются неоднозначными.

Ключевые слова: объем шейки матки; ультразвуковая диагностика; индуцированные роды; естественные роды; кесарево сечение.
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Для цитирования: Кассаянан П., Нонтапром К., Чантабал П., Танасантумронгсак С., Сунтипап М. Объем шейки матки, оцененный по ультразвуковому исследованию, как предиктор успешной родовой деятельности: систематический обзор и метаанализ. Сеченовский вестник. 2025; 16(3): 4–16. Epub ahead of print 17.09.2025. https://doi.org/10.47093/2218-7332.2025.1223

КОНТАКТНАЯ ИНФОРМАЦИЯ:
Сунтипап Мончай, врач и преподаватель кафедры акушерства и гинекологии Университета Сринакаринвирот.
Адрес: ул. Сукхумвит 23, д. 114, район Ваттана, г. Бангкок, 10110, Таиланд
E-mail: monchai@g.swu.ac.th

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Доступ к данным исследования. Данные, подтверждающие выводы этого исследования, можно получить у авторов по обоснованному запросу. Данные и статистические методы, представленные в статье, прошли статистическое рецензирование редактором журнала – сертифицированным специалистом по биостатистике.
Конфликт интересов. Авторы заявляют об отсутствии конфликта интересов.
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Abbreviations:
CD – cesarean delivery
CI – confidence interval
IOL – induction of labor
MD – mean difference
OR – odds ratio
VD – vaginal delivery

HIGHLIGHTS	КЛЮЧЕВЫЕ ПОЛОЖЕНИЯ
Smaller cervical volumes associate with successful vaginal delivery within 24 hours and aligns with earlier achievement of the active phase, but not with overall IOL success across studies.	Меньший объем шейки матки ассоциирован с наступлением естественных родов в течение 24 часов, а также с более ранним вступлением в активную фазу родов, однако связь не подтверждается в отношении общей эффективности индукции родов.
Differences in time-based outcome definitions and measurement techniques (2D vs 3D) underpin substantial between-study variability.	Выраженная гетерогенность исследований обусловлена различиями во временных критериях определения исходов и в методиках измерения объема шейки матки (2D vs 3D).
Cervical volume may be most informative when interpreted alongside established clinical and sonographic factors; standardized measurement and prespecified time windows in larger, geographically diverse cohorts could clarify its incremental predictive value.	Информативность оценки объема шейки матки максимальна при комплексной оценке совместно с клиническими и ультразвуковыми показателями. Для уточнения ее дополнительной прогностической ценности необходима стандартизация методик измерения и проведение многоцентровых исследований на базе географически диверсифицированных когорт с заранее заданными временными интервалами наблюдения.

Induction of labor (IOL) is a common procedure in the field of obstetrics which is aimed at stimulating uterine contractions before the onset of labor to achieve vaginal delivery (VD) [1]. The World Health Organization reported in 2018 that the prevalence of IOL reaches 25% in developed countries[1]. However, IOL can lead to maternal and fetal morbidity and mortality [1]. It increases the risk of emergency cesarean delivery (CD) (odds ratio (OR) 1.89; 95% confidence interval (CI): 1.12 to 3.18) [2], chorioamnionitis (OR 2.6; 95% CI: 2.0 to 3.4) [3], postpartum hemorrhage (OR 1.57; 95% CI: 1.2 to 2.04), and uterine rupture or dehiscence at 1.1% (OR 1.62; 95% CI: 1.13 to 2.31) [4]. These risks emphasize the need for pre-induction assessment to predict successful IOL and minimize adverse outcomes.

The Bishop score is a bedside, pre-induction cervical assessment that sums dilation, effacement, station, position, and consistency to estimate the likelihood of successful IOL. However, because it relies on digital examination rather than objective imaging, it is inherently subjective with notable intra- and inter-observer variability [5, 6], which has driven interest in ultrasound-based pre-induction assessments. Ultrasonographic cervical assessment is performed to assess pre-induction cervical ripening. Common sonographic parameters for predicting IOL success include cervical length, uterocervical angle, and cervical elastography which represents cervical stiffness.

Ultrasonographic cervical assessment shows promise, but prior studies report variable results, so its predictive value for IOL outcomes is not fully established [7–11]. Cervical volume, an alternative novel sonographic measure, may be a predictor of successful IOL. However, its efficacy in predicting successful IOL has not yet been thoroughly explored or reviewed.

Aim of the study: to compare the cervical volume of patients who underwent successful and failed IOL procedures.

MATERIALS AND METHODS

This systematic review and meta-analysis were conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) extension statement for reporting systematic reviews incorporating meta-analysis [12]. Preliminary data was presented at an international conference[2].

Information sources

The databases search was performed covering all available studies, conference proceedings, dissertations, and theses published between January 01, 2005 and December 31, 2024. The studies were identified in PubMed, EMBASE, Scopus, and via manual searches using Google Scholar. The final search was conducted on March 28, 2025.

Eligibility criteria and search strategy

Search terms were developed based on the PECOS framework (population, exposure, comparator, outcomes, and study design)[3]. The full search strategy is presented in Supplement 1 (Supplementary materials on the journal's website https://doi.org/10.47093/2218-7332.2025.1223-annex).

Inclusion criteria:

- Population: pregnant women who underwent IOL;
- Exposure: the measurement of cervical volume using ultrasonography via any route (transabdominal,

[1] WHO recommendations on induction of labour, at or beyond term. World Health Organization; 2022. p 43 (access date: 01.11.2024).

[2] Kassayanan P., Chantabal P., Suntipap, M. Ultrasonography cervical volume as a predictor of successful induction of labor in pregnant women with induction of labor, A systematic review and Meta-analysis. Procedia of Multidisciplinary Research. 2024. 2(10): 99.

[3] Collaboration for environmental evidence. Guidelines and standards for evidence synthesis in environmental management. Pullin AS, GK Frampton, B Livoreil & G Petrokofsky, editors. 2022. http://www.environmentalevidence.org/information-for-authors (access date: 31.07.2025).

transvaginal, or transperineal), with or without a specified cut-off value;
- Comparator: cervical volume threshold (for studies with a cut-off value);
- Outcome: at least one definition of successful IOL, characterized by: VD without a specified timeframe, VD within 24 hours, and achievement of the active phase of labor within 12 hours;
- Study design: cohort studies.

Non-inclusion criteria:
- Non-English languages that were untranslatable;
- The insufficient data for analysis despite three contact attempts with the authors spaced two weeks apart.

Selection process

Studies were manually and independently screened by two reviewers (P.K. and P.C.) based on the titles and abstracts, without the use of automation tools. The full articles were subsequently reviewed to confirm inclusion. Any disagreements were resolved through discussion with a third reviewer (M.S.).

Data collection process

Data was collected independently by two reviewers (P.K. and P.C.) using a standardized data extraction form. Extracted data comprised 6 sections: general study information, study characteristics, participant characteristics, ultrasonographic cervical volume assessment details, outcome summaries, and data for pooling. Study characteristics included the extraction date, author name, study location, ultrasound type and name of ultrasound machine, route of ultrasound, cervical volume measurement methods, participant demographics, method of IOL, indications of IOL, pregnancy complications, ultrasonographic cervical volume, and outcomes of IOL. The researchers classified 'CD,' 'not achieving VD,' and 'no achievement of the active phase of labor' as failed IOLs to avoid inconsistency.

Risk of bias assessment

Two reviewers (P.K. and P.C.) independently assessed the risk of bias in the studies using the modified Newcastle-Ottawa scale, a validated tool for assessing the quality of non-randomized studies[4]. This scale evaluates three domains of bias: selection of the representativeness of the study participants, comparability between groups, and ascertainment of outcomes and study factors. Each item contains a question with three possible answers: yes, no, or unclear. The scale assigns scores ranging from 0 to 9 stars. Individual studies were categorized according to these stars; those with 7 to 9 stars were classified as having a low risk of bias, those with 4 to 6 stars as having a moderate risk of bias, and those with 0 to 3 stars as having a high risk of bias. The third reviewer (M.S.) resolved any disagreements.

Data analysis

Data for pooling was divided into two types: cut-off data and frequency data. For studies with a cut-off, a comparator was implicitly defined (e.g., cervical volume above vs below the threshold), and the data were analyzed as binary outcomes using OR with 95% CI. For studies without a cut-off, cervical volume was considered as a continuous variable, and the data were pooled using mean difference (MD) with 95% CI. The cervical volume data was converted to mean and standard deviation when reported as a median, range, or interquartile range [13]. A random-effects meta-analysis was performed to account for potential heterogeneity across the trials. Leave-one-out sensitivity analyses were performed to assess the robustness of pooled estimates. Heterogeneity was assessed using Cochran's Q test and Higgins's I^2 statistic, where an I^2 more than 50% was considered indicative of substantial heterogeneity [14]. Meta-regression and subgroup analyses were pre-specified to explore potential sources of heterogeneity, including outcome definitions, measurement techniques (2D vs 3D), ultrasound route, parity, IOL indications, and geographic region. Publication bias was evaluated using Deeks' funnel plot and Egger's test [15]. A two-sided p-value <0.05 was considered statistically significant, except for the heterogeneity of Egger's tests, where a p-value <0.1 was used. The statistical analyses were conducted using STATA software package, version 18.0. (Stata Corp, College Station, Texas, USA).

RESULTS

Study selection

Data were collected from three databases: EMBASE, MEDLINE, Scopus, and from Google Scholar. Studies from the reference lists of reviews, protocols, abstracts, and grey literature were also searched and selected. In total, 1396 eligible studies were included. Among these, 48 were excluded due to duplication. After screening the titles and abstracts, seven studies met the inclusion criteria and were incorporated into the final meta-analysis (Fig. 1).

Study characteristics

Seven prospective cohort studies [16–22] involving 534 pregnant women evaluated cervical volume via ultrasonography to predict successful IOL were included. Five studies [16, 18–21] collected data primarily from Asia, whereas one study collected data from Africa [20] and one study from Europe [17]. One study [16] did not report the baseline characteristics of pregnant women. Sample sizes ranged from 36 to 126 participants per

[4] Wells GA, Shea B, O'Connell D, Peterson J, Welch V, Losos M, et al. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. 2000. https://www.ohri.ca/programs/clinical_epidemiology/oxford.asp (access date: 04.11.2024).

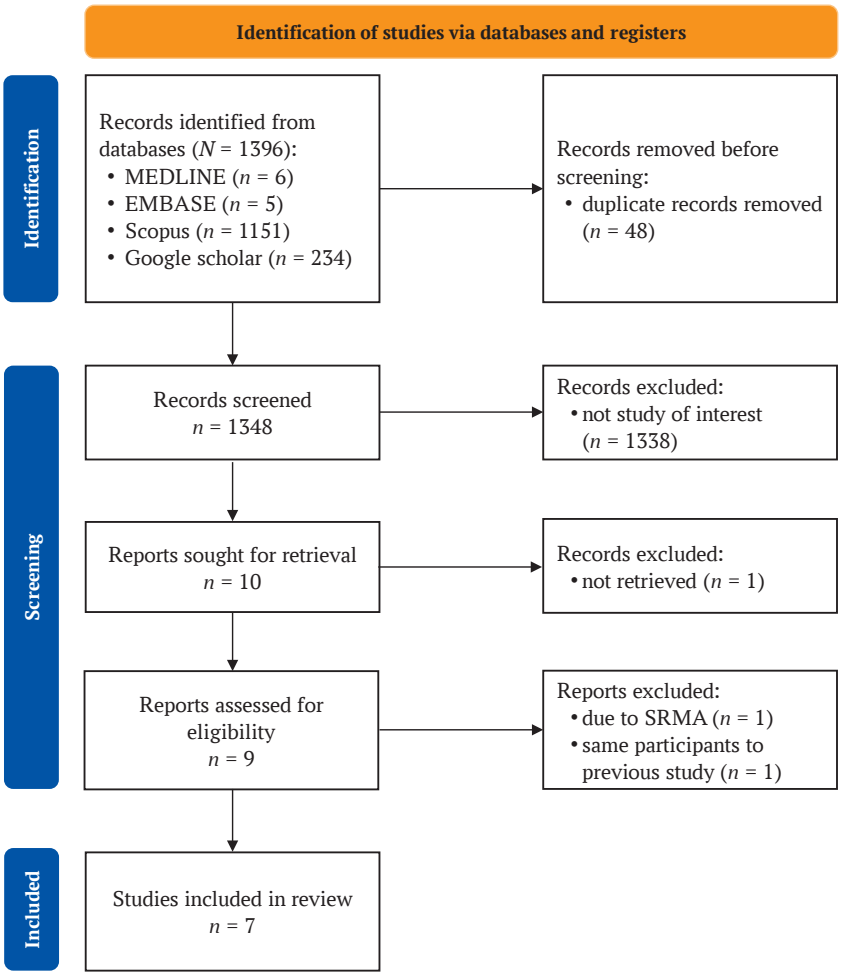


FIG. 1. PRISMA flowchart.

Note: SRMA – systematic review and meta-analysis.

study (Table 1**)**. Cervical volume was measured using two techniques: four studies employed three-dimensional ultrasonography using the Virtual Organ Computer-aided Analysis (VOCAL) software, while two studies utilized two-dimensional ultrasonography applying the cylinder volume formula ($\pi R^2 h$). Five studies used transvaginal ultrasonography, one study used translabial ultrasonography, and the ultrasound approach used in one study was not specified. Two studies reported a specific cervical volume cut-off value to predict successful IOL. The definitions of successful IOL varied across studies. Six studies defined successful IOL as VD, including four studies defined success as achieving VD within 24 hours and three studies defined success as achieving VD without a time limit. Two studies defined it as attaining the active phase of labor within 12 hours (Table 1**)**.

The details of the patients' characteristics and IOL methods are available for six eligible studies (Table 2). The mean age of participants across studies ranged from 25.7 to 33.0 years and the mean body mass index – from 24.0 to 30.5 kg/m^2. The mean gestational age varied between 37.7 and 42.3 weeks, and the mean estimated fetal weight – from 3174 to 3346 grams. Two studies enrolled only nulliparous women. Regarding the IOL methods, one study used only prostaglandin E1, four studies used prostaglandin E2, one study used prostaglandin E2 and a Foley's catheter.

Risk of bias in studies

Risk of bias assessment could not be performed in one study [16] due to unavailability of the full-text article. Among the remaining studies, four studies [17, 20–22] were considered low risk of bias (Fig. 2). Whereas two studies were regarded as high risk of bias: one study [18] raised concerns in the domains of ascertainment of exposure, follow-up period adequacy, and comparability, while another study [20] identified a high risk in the representativeness of the exposed cohort, ascertainment of exposure, and comparability.

Indication for induction of labor

Six studies reported the indications for IOL (Table 3). Among IOL, pregnancy-induced hypertension demonstrated a median prevalence of 11.45%, gestational

Table 1. **Key characteristics of included studies**

Author, year	Sample size	VD/CD	Definition of successful IOL	Cervical volume cut-off value, cm^3	Ultrasound (type, name, method, route)
Rovas, 2005[a]	36	23/13	VD 24 hours	NA	3D, Voluson 730, VOCAL, TVS
Rovas, 2005[a]	36	32/4	Achieved active phase of labor 12 hours	NA	3D, Voluson 730, VOCAL, TVS
Kim, 2010	41	30/11	Achieved active phase of labor 12 hours	NA	3D, Accuvix XQ, Medison, VOCAL, TVS
Young, 2014	126	88/38	VD	NA	NA
Esin, 2016[a]	38	29/9	VD	NA	3D, Volson, VOCAL, TLS
Esin, 2016[a]	29	20/9	VD 24 hours	NA	3D, Volson, VOCAL, TLS
Athulathmudali, 2021	100	63/37	VD 24 hours	28.5	2D, Medison, cylinder volume formula, TVS
İleri, 2023	125	93/32	VD	NA	3D, NA, VOCAL, TVS
Elsheikh, 2024	68	37/31	VD 24 hours	27.0	2D, NA, 2D, Medison, cylinder volume formula, TVS

Notes: [a] two different outcomes were accessed in the study.
CD – cesarean delivery (failed IOL); IOL – induction of labor; NA – not available; TLS – translabial ultrasound; TVS – transvaginal ultrasound; VD – vaginal delivery (successful IOL); VOCAL – Virtual Organ Computer-Aided Analysis; 2D – two-dimensional view; 3D – three-dimensional view.

Table 2. **Baseline characteristics of participants**

Author, year	Mean age, year	Mean BMI, kg/m^2	Nulliparous, %	Mean GA, weeks	Mean EFW, g	IOL method %	Foley, %
Rovas, 2005	33.0	30.5	47	42.3	NA	PGE_1 (100)	NA
Kim, 2010	28.5	26.6	100	37.7	3174	PGE_2 (100)	NA
Young, 2014	NA	NA	100	NA	NA	NA	NA
Esin, 2016	25.7	30.4	50	41.0	3346	PGE_2 (69.6)	30.4
Athulathmudali, 2021	28.4	24.0	71	39.9	3071	PGE_2 (100)	NA
İleri, 2023	27.6	28.7	50.4	38.8	3179	PGE_2 (100)	NA
Elsheikh, 2024	25.7	26.9	NA	38.9	3181	PGE_2 (100)	NA

Note: BMI – body mass index; EFW – estimated fetal weight; GA – gestational age; IOL – induction of labor; NA – not available; PGE_1 – prostaglandin E1; PGE_2 – prostaglandin E2.

Table 3. **Indication for induction of labor of included studies**

Author, year	PIH, %	GDM, %	FGR, %	OHA, %	PTP, %	PROM, %	LGA, %	NRFS, %	MC, %
Rovas, 2005	7.9	NA	7.9	68.4	7.9	NA	7.9	NA	NA
Kim, 2010	14.6	9.8	19.5	4.9	NA	NA	29.3	NA	19.5
Young, 2014	NA	NA	NA	NA	100	NA	NA	NA	NA
Esin, 2016	8.3	NA	8.3	18.8	64.6	NA	NA	NA	NA
Athulathmudali, 2021	6.0	33.0	NA	NA	61.0	NA	NA	NA	NA
İleri, 2023	20.0	7.2	22.4	12.0	21.6	NA	NA	11.2	4.8
Elsheikh, 2024	17.2	7.8	NA	6.3	20.3	28.1	NA	NA	20.3

Note: FGR – fetal growth restriction; GDM – gestational diabetes mellitus; LGA – large for gestational age; MC – maternal condition; NA – not available; NRFS – non-reassuring fetal status; OHA – oligohydramnios; PIH – pregnancy-induced hypertension; PROM – premature ruptured of membrane; PTP – post-term pregnancy.

diabetes mellitus – 8.8%, fetal growth restriction – 13.90%, oligohydramnios – 18.76%, post-term pregnancy – 41.30%, premature ruptured of membrane – 28.1%, large for gestational age – 18.6%, non-reassuring fetal status – 11.2%, maternal condition – 19.5%.

Maternal outcomes

Cervical volume cut-off value and successful VD within 24 hours

Two studies involving 168 pregnant women evaluated cervical volume using different cutoff values of 27 cm^3 and 28.5 cm^3. Pooled analysis demonstrated positive association between lower cervical volume and successful VD within 24 hours (OR 7.19; 95% CI: 3.31 to 15.64; $\tau^2 = 0.00$; $I^2 = 0\%$; 95% predictive interval (approximate, normal-quantile due to only two studies): 3.31 to 15.64; Fig. 3A).

Mean cervical volume and successful VD and CD

Five studies involving 422 pregnant women reported cervical volume without specific cut-off values. Notably, Esin et al. [19] reported data for two predefined outcome definitions: VD without a specified timeframe and VD within 24 hours, which were analyzed separately.

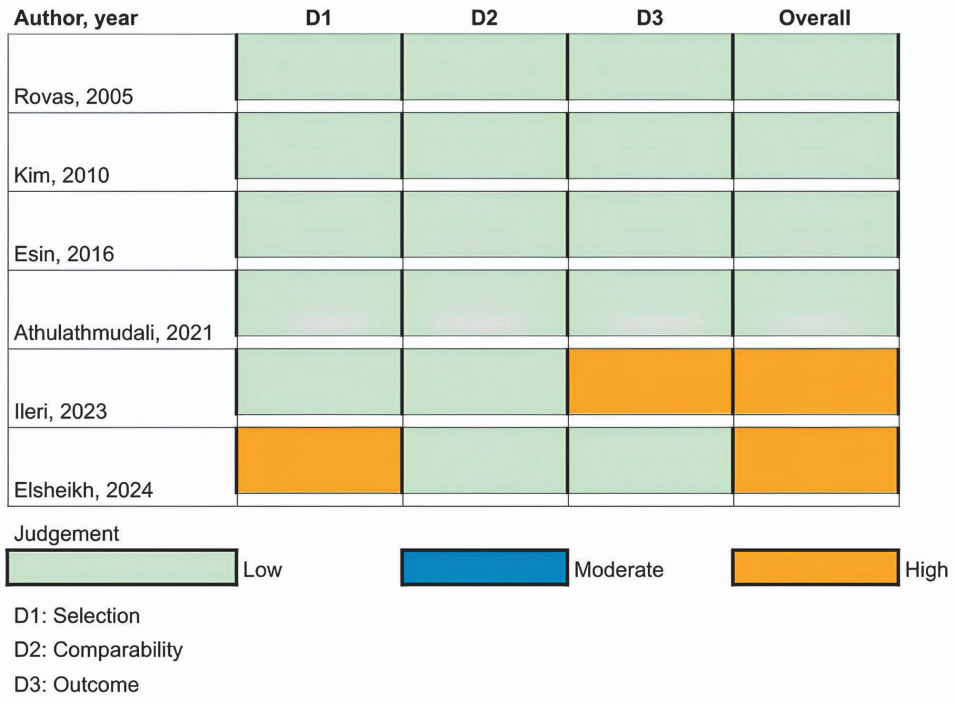


FIG. 2. Traffic light plot for cohort studies using the modified Newcastle–Ottawa scale.

Note: D1 – selection domain; D2 – comparability domain; D3 – outcome domain.

The pooled analysis showed no statistically significant difference between successful and failed IOL (MD −1.32 cm^3; 95% CI: −8.37 to 5.72; I^2 = 89.8%; Fig. 3B). The mean cervical volume in successful IOL ranged from 23.99 with 6.04 cm^3 to 44.17 with 8.66 cm^3, whereas in failed IOL – from 30.1 with 14.7 cm^3 to 48.07 with 11.34 cm^3. Two studies found a significant difference in cervical volume between successful and failed IOL: 36.21 with 9.62 cm^3 vs. 48.07 with 11.34 cm^3 (p < 0.01) [17] and 23.99 with 6.04 cm^3 vs. 29.80 with 7.38 cm^3 (p = 0.02) [22], respectively.

Subgroup analysis

The sources of heterogeneity were explored among the studies using subgroup analysis. Three studies involving 289 pregnant women defined successful IOL as VD without a timeframe. The pooled analysis showed that women with successful VD had a lower mean cervical volume (MD −6.88 cm^3; 95% CI: −14.6 to 0.83 cm^3; I^2 = 83.5%) without a statistically significant difference (Fig. 4A). Exclusion of the outlier study by Young et al. [16] reduced heterogeneity to zero (I^2 = 0%) but did not change the non-significant difference between groups (MD −2.54 cm^3; 95% CI: −6.19 to 1.11; Fig. 4B).

Three studies involving 133 pregnant women defined a successful IOL as a VD within 24 hours. The pooled analysis demonstrated no significant difference between the two groups (MD 5.23 cm^3; 95% CI: 2.27 to 8.19; I^2 = 0; Fig. 4C)

Two studies involving 77 pregnant women defined successful IOL as actively going into labor within 12 hours. Pregnant women who achieved the active phase of labor had a lower mean cervical volume compared with those who did not (MD −5.73 cm^3; 95% CI: −10.64 to −0.81; I^2 = 0%, 95% predictive interval (approximate, normal-quantile due to only two studies): −10.64 to −0.81; Fig. 4D).

Publication bias

Visual inspection of the contour-enhanced funnel plot demonstrated no substantial asymmetry (Fig. 5). Egger's regression test confirmed the absence of small-study effects (coefficient = 0.50, standard error = 1.75, p = 0.78), indicating no evidence of publication bias.

DISCUSSION

This systematic review and meta-analysis evaluate the association between cervical volume and successful IOL. The aggregated data from seven prospective cohort studies suggest that cervical volume, as an objective sonographic parameter, may have a clinically meaningful predictive value in estimating the probability of successful IOL. Specifically, pooled results demonstrate that lower cervical volume cutoff values (less than 27 to 28.5 cm^3) are strongly associated with VD within 24 hours (OR 7.19), although the estimate has wide precision (95% CI: 3.31–15.64).

When compared with the Bishop score for predicting successful IOL, reported ORs for achieving VD within a specified timeframe ranged from 2.15 to 4.22 [6]. Other ultrasonographic cervical parameters demonstrated a similar direction of association. For example, cervical

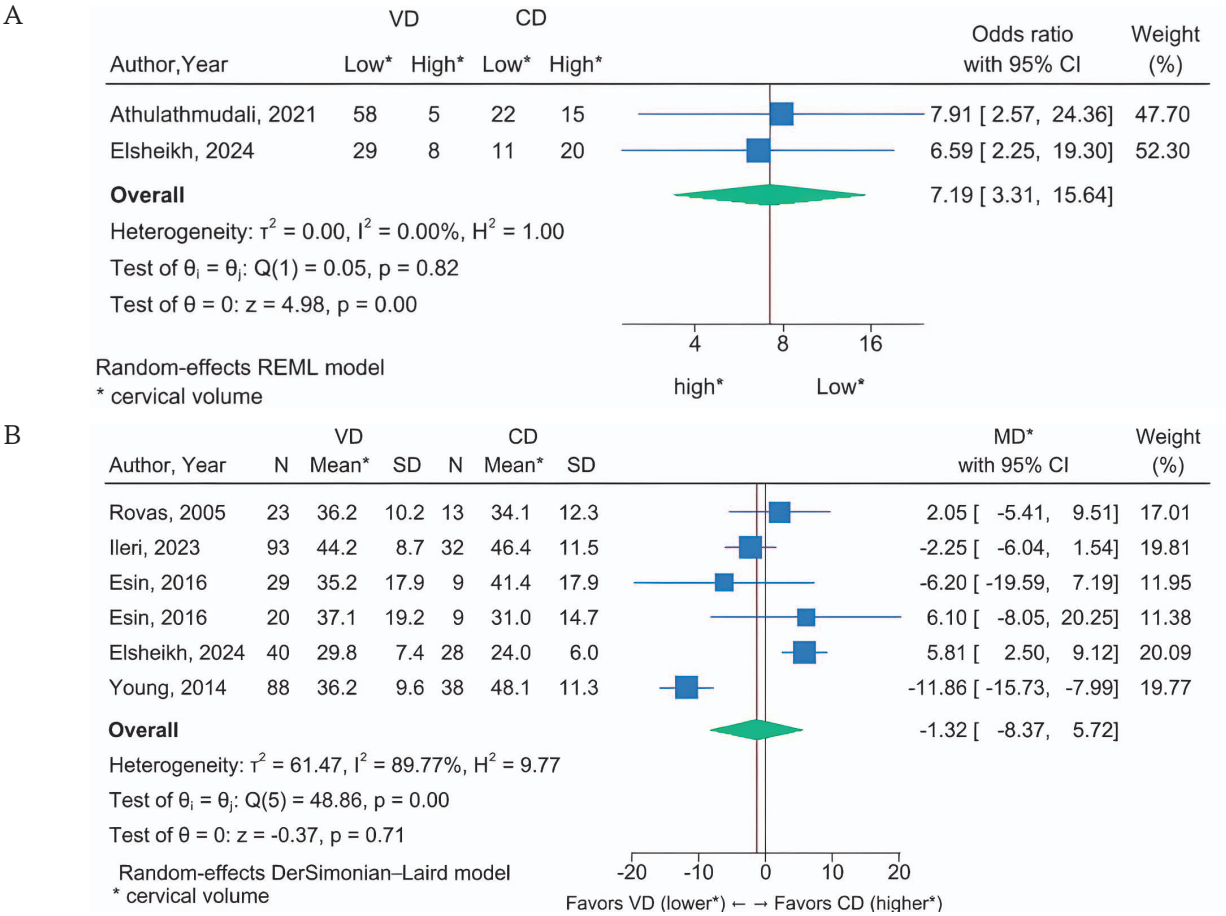


FIG. 3. Forest plots showing weighted effect.
A. Cervical volume cut-off value.
B. Mean cervical volume.

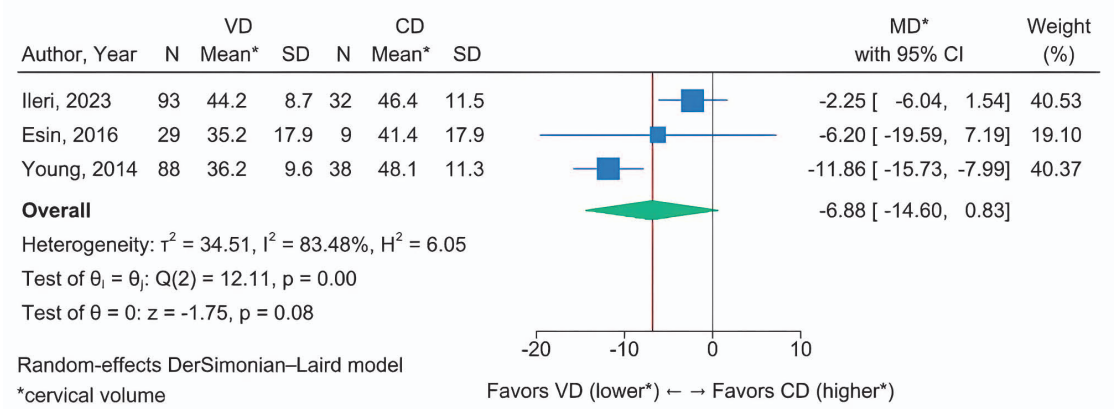
Notes: * cervical volume.
CD – cesarean delivery; CI – confidence interval; MD – mean difference; VD – vaginal delivery.

length with cut-off values of 25 mm, 32 mm, and 40 mm yielded ORs of approximately 5.52, 7.88, and 7.78, respectively, for predicting VD within 24 hours [10]. The presence of cervical wedging was associated with an OR of approximately 2.14 [10], cervical elastography with an OR of 2.97 [8], and the uterocervical angle with an OR of about 4.33 for predicting successful IOL [7]. Based on these findings, cervical volume appears to have a stronger association with successful IOL than other ultrasonographic cervical parameters. However, only two studies [20, 22] provided data on cervical volume, which limits the robustness of this conclusion. In addition, this analysis did not directly compare cervical volume with other ultrasonographic cervical parameters within the same study populations. Variations in the definitions of outcomes, especially differences in the timeframe from induction to delivery, may further reduce the comparability of results across studies.

This review evaluated the criteria for defining the timing of successful IOL as a notable outcome. Studies of cervical volume without cut-off values underwent subgroup analysis for specified versus unspecified time in the VD outcome. Smaller cervical volume was associated with successful VD and the achievement of an active phase within 12 hours. However, the results indicated the opposite for successful VD without timeframe, where larger cervical volume was associated with VD within 24 hours. Therefore, the reliability of these findings may be limited due to the small number of included studies and the possibility that the timeframe used to define successful IOL is overly restrictive. Clinicians evaluating the probability of VD should interpret these results cautiously, as strict time-based definitions, such as requiring VD within 24 hours, may reduce the applicability of the study's results.

Both VD and achievement of the active phase of labor showed a high level of heterogeneity. A subgroup analysis was performed to explore the sources of heterogeneity in the included studies based on the varying definitions of outcomes [23]. When subgrouping by VD without timeframe, I^2 decreased, indicating that one of the sources of heterogeneity was the definition of outcomes

A



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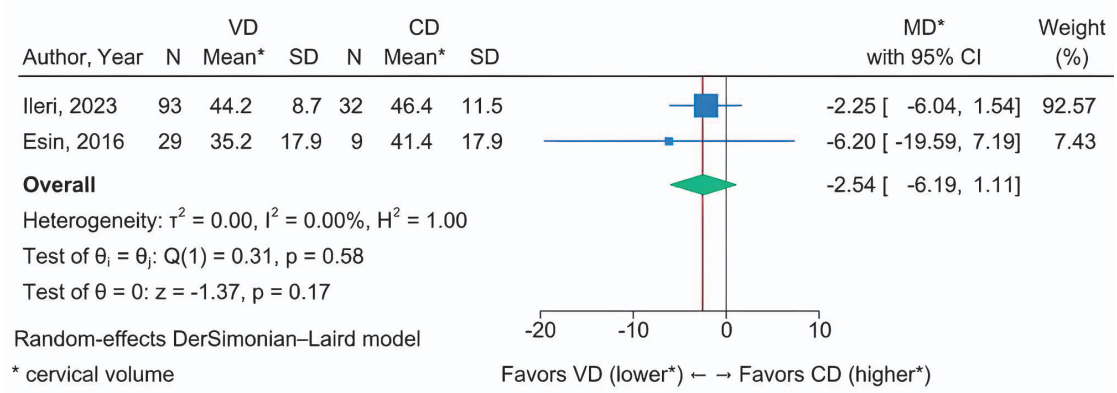

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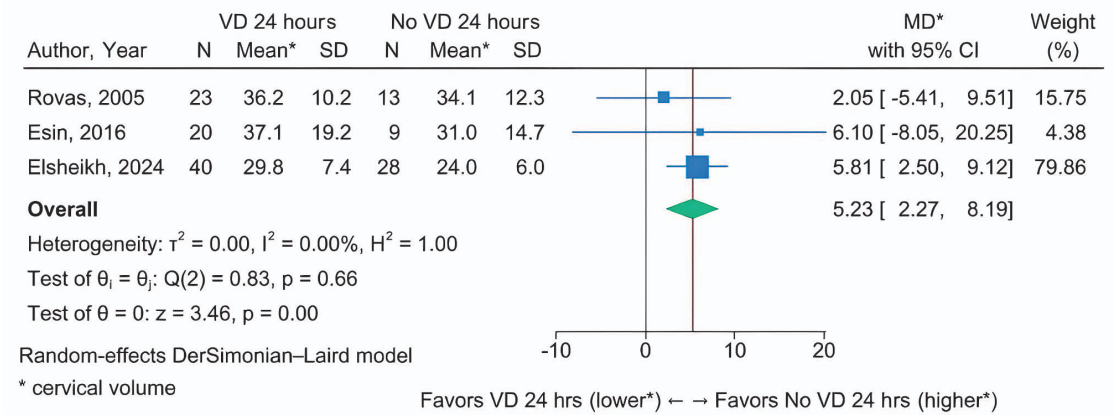

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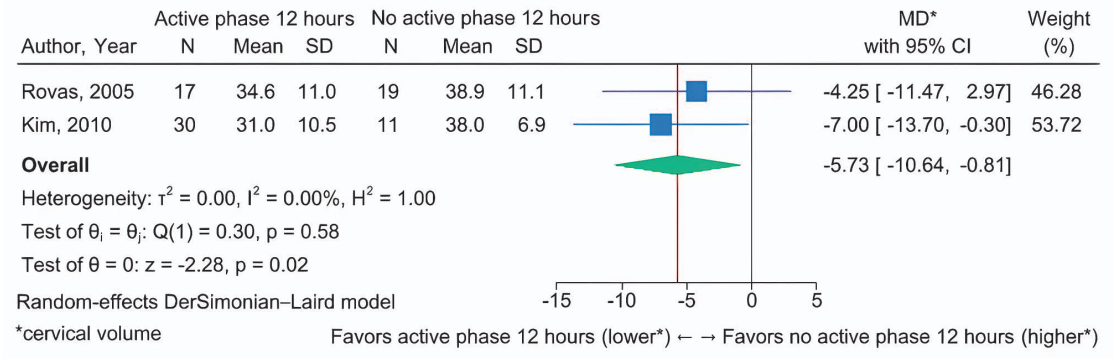

FIG. 4. Forest plots showing subgroup analysis.
A. Outcome without timeframe.
B. Outcome without timeframe (sensitivity analysis).
C. Outcome within 24 hours.
D. Outcome within 12 hours.

Notes: * cervical volume.
CD – cesarean delivery; CI – confidence interval; MD – mean difference; VD – vaginal delivery.

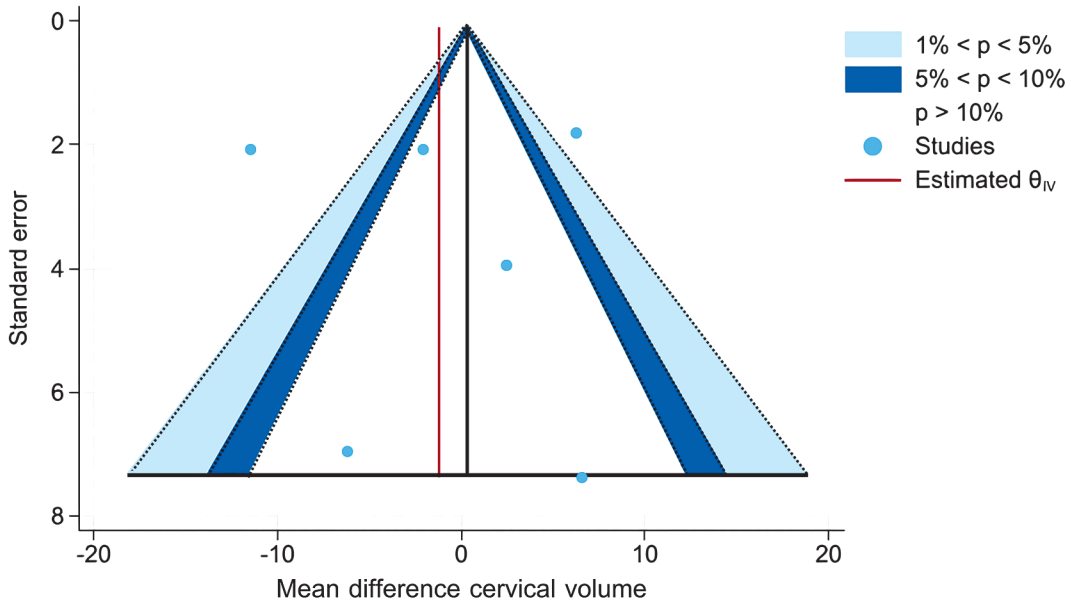

FIG. 5. Funnel plot for a meta-analysis of 7 cohort studies.

within a timeframe. Therefore, the interpretation of the results caused inconsistencies. Additionally, a sensitivity analysis for the outcome of VD within 24 hours was performed by excluding one study [16]; this method could clarify the source of heterogeneity when I^2 was reduced. However, other factors including maternal age, body mass index, gestation age, nulliparity, type of ultrasound, methods of IOL, and indication for IOL, might also have contributed to heterogeneity, because I^2 was not reduced after analysis of these variables.

Furthermore, cervical volume measurement techniques, using either 2D or 3D, influenced the variability of the results in this study. Subgroup analysis of studies employing 2D ultrasonography showed lower heterogeneity than when 2D and 3D were combined. Although 2D cervical volume measurement is simpler and more accessible, it assumes a uniform cylindrical shape of the cervix, which may not precisely reflect cervical anatomy, whereas the 3D technique offers potentially more accurate volume estimation. However, this technique is operator-dependent and requires specific skills and experience, which may contribute to inter-observer variability [24].

For risk of bias assessment, although most observational studies were considered to have a low risk, careful interpretation is still needed, particularly regarding potential issues with cohort comparability and outcome measurements. In terms of publication bias, although Egger's test did not demonstrate a significant small-study effect and the funnel plot appeared generally symmetrical, the ability to detect asymmetry is limited due to the small number of included studies. Therefore, any conclusions that are drawn regarding publication bias should be made cautiously. While contour-enhanced funnel plots help visualize study distribution, any observed asymmetry may reflect true heterogeneity, methodological variation, or selective publication.

This study assessed specific outcomes, including successful VD and achievement of the active phase of labor, and analyzed subgroups by specified versus non-specified timeframe, which provided a more precise context for interpretation and reduced heterogeneity. Although the association among included studies was similar for VD without a timeframe, heterogeneity was substantial, with one study contributing a markedly high MD. A sensitivity analysis was therefore conducted to explore potential sources of heterogeneity. The results indicated that pregnant women with successful VD had a smaller cervical volume than those without. Sources of heterogeneity were further explored based on different clinical definitions to improve consistency. Additionally, inclusion was not restricted to published papers. Other relevant sources were considered to make the evidence base as diverse and comprehensive as possible, reduce the publication bias, and to make sure the findings are as valid as can be.

Limitations of the study

This meta-analysis has several limitations. First, it included only seven studies, rendering it statistically less compelling and reducing the confidence in the pooled estimates. Second, most studies were conducted in Asia, with only one each from Europe and Africa. This geographic imbalance may reflect differences in clinical practice and available resources, which could affect the generalizability of our findings. Third, cervical volume was measured using different ultrasound modalities (2D vs 3D). Currently, no standard method exists, and thus there is an element of measurement variability.

Fourth, some studies had a high risk of bias, especially in exposure ascertainment, follow-up adequacy, and comparability. One study could not be assessed due to the lack of access to the full-text. Fifth, conflicting findings were observed regarding cervical volume and VD, possibly due to the timeframe used (within 24 hours vs any time), which may influence the interpretation. Lastly, substantial heterogeneity was present, likely exacerbated by the small number of included studies. All of these factors should be taken into consideration when interpreting the results. Of course, further research is needed to confirm all these findings.

Directions for further research

This study supports the potential role of cervical volume in predicting successful IOL, but several aspects require further investigation. First, standardized measurement methods should be developed to reduce variability in techniques (e.g., 2D vs 3D, use of VOCAL vs cylinder volume formula, and ultrasound approach), which can affect measurement reliability. Second, studies with larger and more diverse populations are needed to improve generalizability. Third, combining cervical volume with other clinical or sonographic parameters may enhance clinical utility. Finally, research should evaluate the clinical value of cervical volume in routine pre-induction assessments.

CONCLUSIONS

Cervical volume has significant potential as a parameter for predicting successful IOL in decision support frameworks in obstetrics. While some studies report smaller cervical volume being associated with better IOL outcomes, subgroup findings remain inconclusive. Ultrasonography to determine cervical volume can be combined with other clinical maternal and fetal parameters to enhance decision support systems and revolutionize delivery care in obstetrics. Further research using standardized cervical volume measurement methods, larger sample sizes, broader geographic representation, and analyses of pregnant women of the same parity may improve the precision of ultrasonographic cervical volume as a predictor of successful IOL.

AUTHOR CONTRIBUTIONS

Potsanop Kassayanan and Monchai Suntipap developed the concept and design of the study, as well as analyzed and interpreted the data. Potsanop Kassayanan, Prame Chantabal and Monchai Suntipap collected the primary data. Monchai Suntipap performed the statistical analysis. Potsanop Kassayanan, Kasidis Nontaprom, Switta Thanasantumrongsak and Monchai Suntipap drafted the manuscript and took part in the critical revision of the manuscript. All the authors approved the final version of the article.

ВКЛАД АВТОРОВ

П. Кассаянан и М. Сунтипап разработали концепцию и дизайн исследования, участвовали в анализе и интерпретации данных. П. Кассаянан, П. Чантабал и М. Сунтипап участвовали в сборе первичных данных. М. Сунтипап проводил статистический анализ. П. Кассаянан, К. Нонтапром, С. Танасантумронгсак и М. Сунтипап участвовали в подготовке текста и провели критический анализ рукописи. Все авторы одобрили окончательную версию статьи.

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INFORMATION ABOUT THE AUTHORS / ИНФОРМАЦИЯ ОБ АВТОРАХ

Potsanop Kassayanan, student, Faculty of Medicine, Srinakharinwirot University.
ORCID: https://orcid.org/0009-0004-7335-1116

Kasidis Nontaprom, student, Faculty of Medicine, Srinakharinwirot University.
ORCID: https://orcid.org/0009-0003-2917-0601

Prame Chantabal, MD, gynecologist, Department of Obstetrics and Gynecology, Khlong Luang Hospital.
ORCID: https://orcid.org/0009-0000-6517-638X

Switta Thanasantumrongsak, student, Faculty of Medicine, Srinakharinwirot University.
ORCID: https://orcid.org/0009-0009-9346-6611

Monchai Suntipap✉**,** MD, MSc, lecturer, doctor, Department of Obstetrics and Gynecology, Srinakharinwirot University.
ORCID: https://orcid.org/0009-0009-9176-9301

Кассаянан Потсаноп, студент медицинского факультета Университета Сринакаринвирот.
ORCID: https://orcid.org/0009-0004-7335-1116

Нонтапром Касидис, студент медицинского факультета Университета Сринакаринвирот.
ORCID: https://orcid.org/0009-0003-2917-0601

Чантабали Праме, врач-гинеколог отделения акушерства и гинекологии больницы Клонг Луанг.
ORCID: https://orcid.org/0009-0000-6517-638X

Танасантумронгсак Свитта, студент медицинского факультета Университета Сринакаринвирот.
ORCID: https://orcid.org/0009-0009-9346-6611

Сунтипап Мончай✉**,** врач и преподаватель кафедры акушерства и гинекологии Университета Сринакаринвирот.
ORCID: https://orcid.org/0009-0009-9176-9301

✉ Corresponding author / Автор, ответственный за переписку

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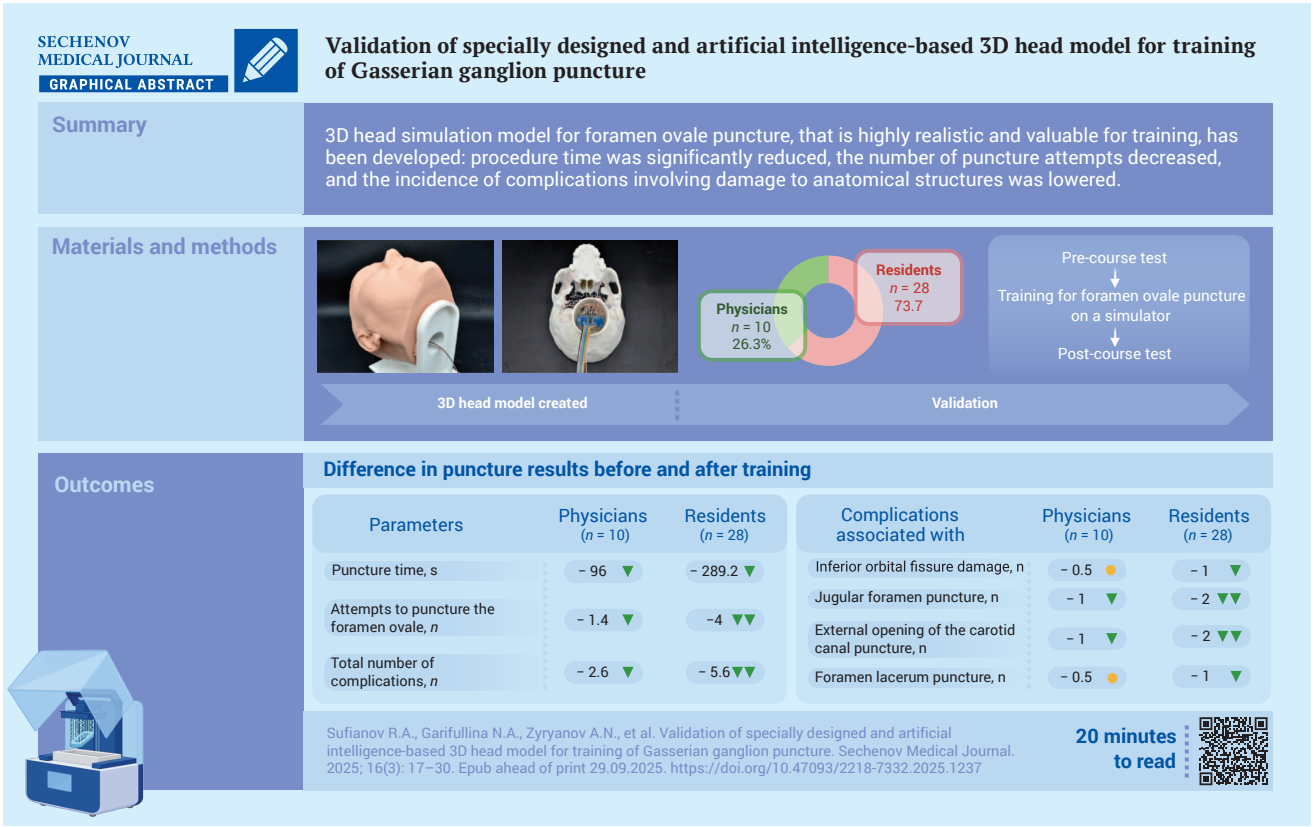
Validation of specially designed and artificial intelligence-based 3D head model for training of Gasserian ganglion puncture

Rinat A. Sufianov[1,2,✉], Nargiza A. Garifullina[1,3,4], Aleksandr N. Zyryanov[3], Anton D. Zakshauskas[3], Margarita F. Chakhmakhcheva[4], Albert A. Sufianov[1,3,5,6]

[1]Sechenov First Moscow State Medical University (Sechenov University)
8/2, Trubetskaya str., Moscow, 119048, Russia
[2]N.N. Blokhin National Medical Research Center of Oncology
24, Kashirskoye Highway, Moscow, 115522, Russia
[3]Federal Center of Neurosurgery (Tyumen)
5, 4 km of Chervishevskogo trakta str., Tyumen, 625032, Russia
[4]Tyumen State Medical University
54, Odesskaya str., Tyumen, 625023, Russia
[5]Peoples' Friendship University of Russia named after Patrice Lumumba
6, Miklukho-Maklaya str., Moscow, 117198, Russia
[6]King Edward Medical University
Anarkali, Lahore, 54000, Pakistan



Abstract

Aim. To design, develop and validate a 3D head simulation model for foramen ovale puncture, incorporating computer vision-based artificial intelligence (AI) technologies.

Materials and methods. A 3D simulation model with AI integration was developed in the prototyping laboratory. Its effectiveness for surgical training was evaluated by two groups: neurosurgeons with five or more years of experience (*n* = 10) and residents (*n* = 28). Training outcomes were assessed using the following parameters: intervention time,

number of puncture attempts until they achieved the first one without any complications, number of complications involving critical anatomical structures. The validity was assessed using a Likert scale.
Results. Before the training session, the groups differed in terms of the time spent on the procedure, the number of puncture attempts and the number of complications involving critical anatomical structures. Post-training intervention time decreased by 50% in both groups, the number of puncture attempts reduced by 50.0% in physicians and by 60.3% in residents. The cumulative number of complications declined by 57.8% in physicians and by 59% in residents. Likert scale analysis revealed no statistically significant differences between groups across all parameters. The feasibility and educational effectiveness of the model were rated as 4 or 5 by 90% of participants in both groups. Anatomical realism received a score of 4 or 5 from 90% of physicians and 100% of residents. Radiographic realism received a score of 4 or 5 from all participants. The cost of creating a simulator, excluding the cost of a 3D printer, was 22,685 rubles.
Conclusion. The developed 3D simulation model with AI integration significantly improved training outcomes both in physicians' and residents' groups. The use of standard prototyping equipment provides a cost-effective, radiation-free alternative for widespread implementation in neurosurgical education.

Keywords: computer vision; 3D reconstruction; simulation model; foramen ovale; trigeminal neuralgia; neuronavigation system
MeSH terms:
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CONTACT INFORMATION:
Rinat A. Sufianov, Cand. of Sci. (Medicine), Associate Professor, Department of Neurosurgery, Sechenov First Moscow State Medical University (Sechenov University); neurosurgeon, Department of Neurooncology, N.N. Blokhin National Medical Research Center of Oncology.
Address: 8/2, Trubetskaya str., Moscow, 119048, Russia
E-mail: rinat.sufianov@gmail.com

Ethics statements. The study was conducted in accordance with the permission of the Local Ethics Committee of Sechenov First Moscow State Medical University (Sechenov University), No 10-25 dated April 24, 2024.
Data availability. The data confirming the findings of this study are available from the authors upon reasonable request. Data and statistical methods used in the article were examined by a professional biostatistician on the Sechenov Medical Journal editorial staff.
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Валидация специально разработанной 3D-модели головы с применением искусственного интеллекта для обучения пункции гассерова узла

Р.А. Суфианов[1,2,✉], Н.А. Гарифуллина[1,3,4], А.Н. Зырянов[3], А.Д. Закшаускас[3], М.Ф. Чахмахчева[4], А.А. Суфианов[1,3,5,6]

[1]ФГАОУ ВО «Первый Московский государственный медицинский университет имени И.М. Сеченова» Министерства здравоохранения Российской Федерации (Сеченовский Университет)
ул. Трубецкая, д. 8, стр.2, г. Москва, 119048, Россия
[2]ФГБУ «Национальный медицинский исследовательский центр онкологии имени Н.Н. Блохина» Министерства здравоохранения Российской Федерации
Каширское шоссе, д. 24, г. Москва, 115522, Россия
[3]ФГБУ «Федеральный центр нейрохирургии» Министерства здравоохранения Российской Федерации (г. Тюмень)
4-й км Червишевского тракта, д. 5, г. Тюмень, 625032, Россия
[4]ФГБОУ ВО «Тюменский государственный медицинский университет» Министерства здравоохранения Российской Федерации
ул. Одесская, д. 54, г. Тюмень, 625023, Россия
[5]ФГАОУ ВО «Российский университет дружбы народов имени Патриса Лумумбы»
ул. Миклухо-Маклая, д. 6, г. Москва, 117198, Россия
[6]Медицинский университет короля Эдуарда
Анаркали, г. Лахор, 54000, Пакистан

Аннотация

Цель. Спроектировать, разработать и валидировать 3D-модель головы для пункции овального отверстия, используя технологии искусственного интеллекта (ИИ) на основе компьютерного зрения.

Материалы и методы. В лаборатории прототипирования разработана трехмерная симуляционная модель с интеграцией ИИ. Ее эффективность для хирургического обучения оценивалась в двух группах: нейрохирурги с опытом работы пять и более лет (n = 10) и ординаторы (n = 28). Результаты обучения оценивались по времени вмешательства, количеству попыток пункции до первой попытки без осложнений, количеству осложнений, связанных с повреждением критических анатомических структур. Валидность оценивалась с помощью шкалы Лайкерта.

Результаты. До обучения группы различались по времени, затраченному на вмешательство, количеству попыток пункции и количеству осложнений, связанных с повреждением критических анатомических структур. После обучения время вмешательства сократилось на 50% в обеих группах, количество попыток пункции уменьшилось на 50,0% у врачей и на 60,3% у ординаторов. Общее число осложнений снизилось на 57,8% у врачей и на 59% у ординаторов. Анализ шкалы Лайкерта не выявил статистически значимых различий между группами по всем параметрам. Осуществимость и образовательная эффективность модели были оценены на 4 или 5 баллов 90% участников в обеих группах. Анатомическая реалистичность получила оценку 4 или 5 у 90% врачей и 100% ординаторов. Рентгенографический реализм получил оценку 4 или 5 от всех участников. Стоимость создания симулятора, не учитывая стоимость 3D-принтера, составила 22 685 рублей.

Заключение. Разработанная 3D-симуляционная модель с интеграцией искусственного интеллекта значительно улучшила результаты обучения как в группе врачей, так и в группе ординаторов. Использование стандартного оборудования для прототипирования представляет собой экономически эффективную, безрадиационную альтернативу для широкого внедрения в нейрохирургическое образование.

Ключевые слова: компьютерное зрение; 3D-реконструкция; симуляционная модель; овальное отверстие; невралгия тройничного нерва; система нейронавигации

Рубрики MeSH:
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ТРОЙНИЧНОГО НЕРВА НЕВРАЛГИЯ – ТЕРАПИЯ

ТРОЙНИЧНОГО НЕРВА ГАНГЛИЙ – ДИАГНОСТИЧЕСКОЕ ИЗОБРАЖЕНИЕ
ТРОЙНИЧНОГО НЕРВА ГАНГЛИЙ – ХИРУРГИЯ
ПУНКЦИИ – МЕТОДЫ
ТРЕХМЕРНОГО ИЗОБРАЖЕНИЯ ПОСТРОЕНИЕ
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КОНТАКТНАЯ ИНФОРМАЦИЯ:
Суфианов Ринат Альбертович, кандидат медицинских наук, доцент кафедры нейрохирургии ФГАОУ ВО «Первый МГМУ им. И.М. Сеченова» Минздрава России (Сеченовский Университет); врач-нейрохирург отделения нейроонкологии ФГБУ «НМИЦ онкологии им. Н.Н. Блохина» Минздрава России.
Адрес: ул. Трубецкая, д. 8, стр. 2, г. Москва, 119048, Россия
E-mail: rinat.sufianov@gmail.com

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Доступ к данным исследования. Данные, подтверждающие выводы этого исследования, можно получить у авторов по обоснованному запросу. Данные и статистические методы, представленные в статье, прошли статистическое рецензирование редактором журнала – сертифицированным специалистом по биостатистике.
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Abbreviations:
AI – artificial intelligence
FO – foramen ovale
GG – Gasserian ganglion

HIGHLIGHTS	КЛЮЧЕВЫЕ ПОЛОЖЕНИЯ
The usage of the Inobitec DICOM Viewer software and Autodesk 3D Max software packages allows you to develop an individual simulator based on the initial MRI and CT DICOM data of the patient for preoperative training foramen ovale puncture in trigeminal neuralgia.	Использование программных пакетов Inobitec DICOM Viewer software и Autodesk 3D Max software позволяет разработать индивидуальный симулятор на основе исходных DICOM данных пациента, полученных при магнитно-резонансной и компьютерной томографии, для предоперационной отработки пункции овального отверстия при невралгии тройничного нерва.
The usage of a conductive filament and an electroactive puncture needle provides immediate feedback, effectively minimizing the risk of the developing incorrect skills in case of trajectory deviation of the puncture needle.	Использование токопроводящего филамента и электроактивной пункционной иглы обеспечивает немедленную обратную связь, что эффективно предотвращает формирование неправильных навыков в случае девиации траектории пункционной иглы.
After training on the simulator undertaken by neurosurgeons (with more than 5 years of experience) and residents, the intervention time, the number of puncture attempts and the frequency of complications significantly decrease.	После обучения на симуляторе нейрохирургов (с опытом более 5 лет) и ординаторов значимо снижается время вмешательства, количество попыток пункции и частота осложнений.

The paradigm of a competency-based surgical education is intrinsically linked to the structured training of specialists [1]. A key strategy for preparing neurosurgical trainees involves combining rigorous theoretical instruction with accessible practical experience [2]. Today, challenges in literature accessibility are largely addressed through global open-access archives of medical publications [3]. However, the limited duration of residency and the potential for fatal complications arising from intraoperative neurosurgical

errors constrain the acquisition of hands-on surgical skills [4].

In the current literature, little attention is paid to simulation models for training puncture techniques in the treatment of trigeminal neuralgia [5]. D.B. Almeida et al. [6] described a method for creating a model for practicing puncture treatment of trigeminal neuralgia based on a cadaveric skull, in which the authors used a skull with a movable lower jaw actuated by springs, preserved spatial dimensions for the silicone structure, and applied a latex mask to enhance realism. A similar model based on a cadaveric skull was presented by Y.Q. He et al. in 2014 [7], with the distinctive feature of incorporating a silicone Gasserian ganglion (GG).

While cadaveric dissection remains the gold standard for technical training, legal, ethical, and financial constraints have led to a yearly decline in cadaver availability [5]. The active integration of artificial intelligence (AI) and engineering technologies in medicine has transformed approaches to surgical education [8].

The procedural target in trigeminal neuralgia punction is the GG, which is most safely and effectively accessed via the foramen ovale (FO) of the skull base [9]. Performing GG puncture under radiologic guidance requires additional hand-eye coordination, as it relies on fluoroscopic trajectory alignment without direct visual feedback. However, fluoroscopic guidance limits training time due to the negative effects of ionizing radiation [10]. Emulating C-arm functionality via computer vision technologies can offer a safe and accessible training solution.

Aim of the study: to design, develop and validate a 3D head simulation model for FO puncture, incorporating computer vision-based AI technologies.

MATERIALS AND METHODS

This study consisted of two parts: the design of a 3D head model using AI (01.05–17.06.2024), and the evaluation of its training validity (15.08–01.10.2024).

Part 1. Development of the 3D head model

Pseudonymized magnetic resonance imaging and computed tomography data in DICOM format from one patient with trigeminal neuralgia were utilized to construct the 3D model. A detailed research protocol was developed to guide the modeling of specific anatomical structures: cerebral arteries (based on 3D time of flight magnetic resonance angiography), cranial nerves (fast Spoiled Gradient Echo based on magnetic resonance imaging), and the skull (computed tomography imaging).

Using the Inobitec DICOM Viewer software (Inobitec DICOM Viewer Pro licensed software, Inobitec LLC, Russia), artifact removal and segmentation were performed for the following structures based on native DICOM data: the skull base, contact zones in the skull base region (including the inferior orbital fissure, jugular foramen, external opening of the temporal carotid canal, lacrimal foramen and spinous foramen), GG, and internal carotid artery (Fig. 1A).

The segmented data were exported in STL format to Autodesk 3D Max software (3ds Max licensed software, Autodesk Inc., USA), where the following elements were modeled: a hinge mechanism to simulate the mobility of the temporomandibular joint, GG (including maxillary, mandibular, and orbital branches), a non-anatomical Meckel's cave (a cavity within the GG aligned with the triangular plexus projection), a tube for housing electronic components, a stand for the 3D head model, a LED screen, negative skin molds for silicone casting, and custom molds for silicone containers (Fig. 1B–F).

Autodesk 3ds Max data were exported to PrusaSlicer software (open-source license, Prusa Research, Czech Republic) to prepare for printing on a Hercules Strong DUO 3D printer (IMPRINTA Russia) with a TwinHot dual extruder head, using fused deposition modeling technology. The resulting file was saved in GCODE format.

Two extruders were used simultaneously to fabricate the skull base. The first extruder, loaded with white ABS plastic, printed the main non-electroactive volume of the skull with 100% filling to simulate the density of the bone structure. The second extruder used electrically conductive black filament U3 Flex Conductive to print the electroactive areas of the skull. The conductive properties of the material were achieved through its composition, which included thermoplastic polyurethane and carbon nanotubes. In addition, 3D models of internal carotid artery and GG were printed using the conductive filament. In contrast, components such as the electronic tube housing, the head model stand, LED screen frame, negative skin molds for silicone casting, and negative molds for tip production were printed with PLA plastic.

To create skin models, the printed silicone molds were treated with a wax-based release spray lubricant. For casting, Ecoflex 00-10, a platinum-based silicone system, was mixed with POLYMER O coloring pigment paste and degassed using a vacuum compressor prior to pouring. The silicone system was poured into the prepared mold. The skin model was bonded to the skull using SIL-POXY, a silicone-based adhesive. For simulation of the dura mater, the Platset 20 silicone system was applied to the inner surface of the skull model. To recreate the Meckel cavity, the negative tip mold was coated with silicone to form a balloon-like structure, which was fixed to the electronic tube with SIL-POXY adhesive. The silicone tube was connected to a 20 mL syringe that delivered pressurized water.

After preparation of all components, the electroactive zones were connected to the electronic unit with flexible copper fluoroplastic-insulated stranded wires. Light and sound signaling of instrument contact detection with electroactive zones of the skull base, as well as with 3D models of the internal carotid artery and GG, was carried

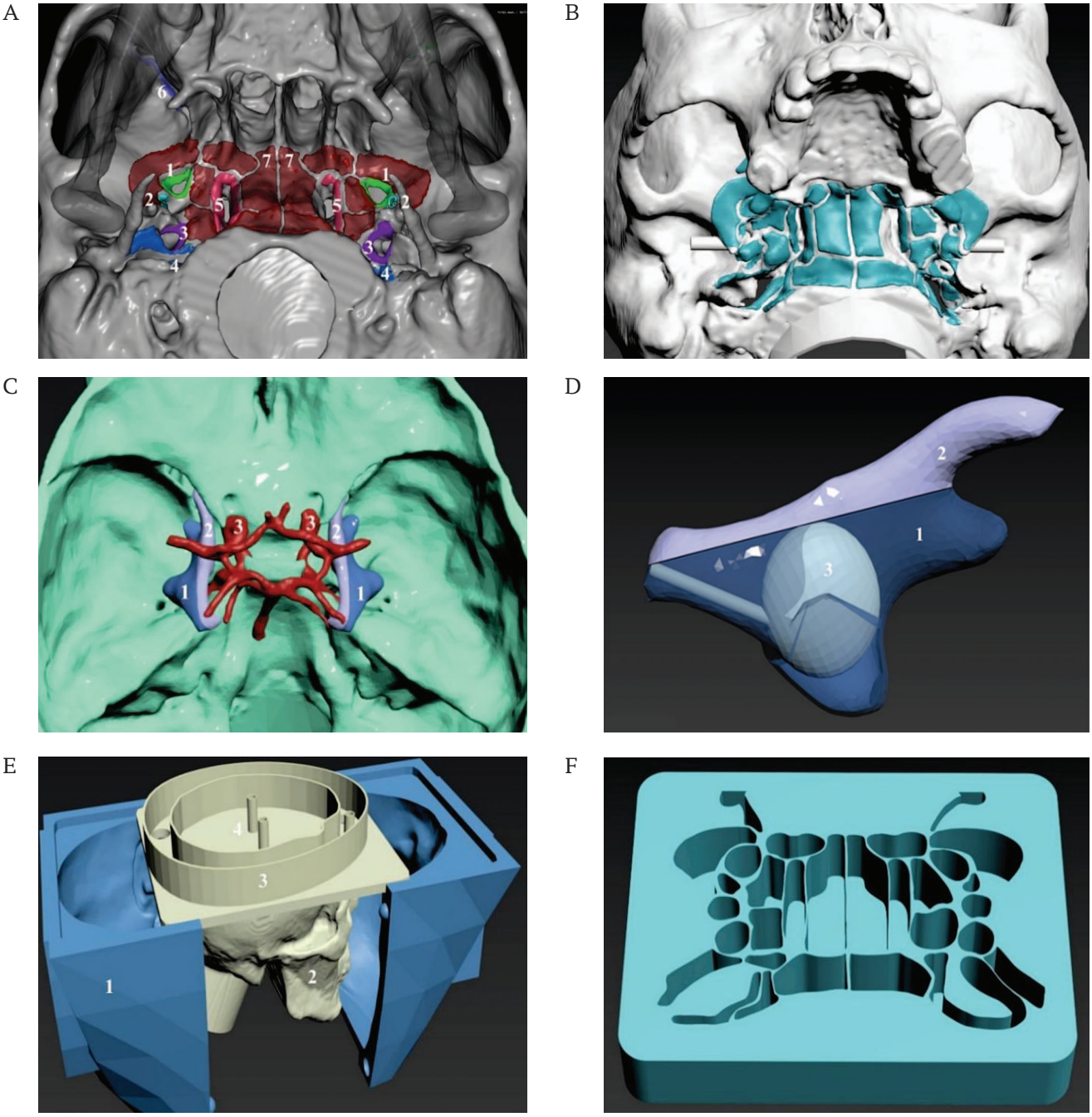

FIG. 1. 3D head model created by Inobitec and Autodesk 3D Max software.
A. The 3D model of the skull base with highlighted contact and non-contact zones (Inobitec software): 1 – foramen ovale (green color), 2 – foramen spinosum (turquoise color), 3 – external opening of the carotid canal (lilac color), 4 – foramen jugulare (blue color), 5 – foramen lacerum (pink color), 6 – inferior orbital fissure (dark blue), 7 – adjacent non-contact zones (red color).
B. The 3D model of the skull base with highlighted contact and non-contact zones (both marked in turquoise, Autodesk 3D Max software).
C. The 3D model of the Gasserian ganglion and internal carotid artery (Autodesk 3D Max software): 1 – maxillary and mandibular zones of the Gasserian ganglion, 2 – ophthalmic branch of the Gasserian ganglion, 3 – internal carotid artery.
D. The 3D model of the Gasserian ganglion with a simulated Meckel's cave (Autodesk 3D Max software): 1 – maxillary and mandibular zones of the Gasserian ganglion, 2 – ophthalmic branch of the Gasserian ganglion, 3 – non-anatomic Meckel's cave (cavity inside the Gasserian ganglion in the triangular plexus projection).
E. The 3D printed form for silicone casting of the external part of the skin in collapsible mold (Autodesk 3D Max software): 1 – 3D printed model of the negative mold for skin filling, 2 – 3D model of the skull for skin filling, 3 – container for additional volume of silicone, 4 – ventilation holes for degassing.
F. The 3D model of the LED screen (Adobe 3D Max software).

out by detecting electrical resistance in the "conductive plastic – puncture needle" circuit (Fig. 2A–F).

In addition to the conductivity of the needle, a special QR code was printed and attached to the end of the needle to apply computer vision technology.

The "conductive plastic – puncture needle" circuit was implemented via a programmable multichannel electronic unit based on Arduino Nano microcontroller (open-source hardware and software platforms, Arduino Software, Italy). Expansion of analog input capacity was achieved using a 16-channel multiplexer (CD74HC4067), while output expansion for LED signal indicators was facilitated using 74HC595 shift registers. LED indication was realized by means of SMD 5730 type LEDs and 15 Ohm current-limiting resistors. A circuit diagram of the 3D head model operation based on the ARDUINO microcontroller is presented in Supplement A (Supplementary materials on the journal's website https://doi.org/10.47093/2218-7332.2025.1237-annex-a).

White LEDs, responsible for detection of the skull base zones, were installed at designated positions on the LED screen, each separated by plastic dividers to minimize the scattering of the light flux around the perimeters of certain zones. Additionally, green LED (Led1) and red LED (Led2) were mounted at the base of the LED screen to indicate puncture needle contact with the GG and internal carotid artery, respectively. The total cost of consumables was 22,685 rubles.

The time spent on modeling was 5 days, production of the 3D model – 2 days, work with electronics and programming – 4 days. The total cost of consumables was 22,685 rubles (Supplementary materials on the journal's website https://doi.org/10.47093/2218-7332.2025.1237-annex-b).

Finally, a portable neuronavigation system was developed to reduce radiation exposure for trainees. To simulate the puncture intervention, an integrated hardware-software complex utilizing computer vision technologies was employed. Video tracking of the surgical instrument was achieved by detecting fractal markers in the form of QR codes affixed to the instrument. The streaming image was captured and transferred to a personal computer, where it was processed using the PLUS Server application (open-source software, Plus Toolkit Community and PerkLab) [11]. In this system, AI algorithms convert the incoming video stream into a matrix of spatial coordinates. These coordinates are subsequently transferred to a dedicated visualization platform – 3D Slicer software (open-source license) [12]. The resulting spatial data were mapped onto a virtual environment within 3D Slicer, where the coordinates were assigned to a 3D model of the surgical instrument. This allowed dynamic visualization of its interaction with the 3D training model of the head on the monitor screen. Two essential models were integrated into the 3D Slicer environment: the virtual surgical instrument and the static head model, reconstructed from patient-specific DICOM data. The head model is static, while the surgical instrument moved in real time according to the physical instrument's position, thereby simulating C-arm-like visualization during the simulated procedure (Fig. 3).

Part 2. Validation of the training model of the foramen ovale puncture simulator

A total of 38 participants, 10 experts (neurosurgeons with more than 5 years of experience) of the Federal Center of Neurosurgery (Tyumen) and 28 residents of the Department of Neurosurgery of the Sechenov First Moscow State Medical University (Sechenov University), whose clinical site is located at Federal Center of Neurosurgery, underwent the simulation program (Fig. 4).

Inclusion criteria:

- age from 23 to 60 years;
- theoretical knowledge of the topographic anatomy of the skull base;
- theoretical knowledge of the radiographic orientation of the FO of the skull;
- no prior involvement in the development of the simulation model;
- a written voluntary informed consent to participate in the study.

Non-inclusion criterion:

- mental disorders affecting learning (n = 0).

The training took place in a laboratory setting is presented in the video file Supplement C (Supplementary materials on the journal's website https://doi.org/10.47093/2218-7332.2025.1237-annex-c).

The results of the FO puncture were evaluated before and after training period using the following parameters:

- intervention time;
- number of puncture attempts;
- number of complications during the puncture involving anatomical structures located at the skull base (the inferior orbital fissure, jugular foramen, external opening of the temporal bone carotid canal, foramen lacerum, and foramen spinosum) as well as in the region of the middle cranial fossa (the first branch of the trigeminal nerve and the cavernous segment of the internal carotid artery).

Before and after training, each participant performed a series of puncture attempts until they achieved the first one without any complications. Once this had been achieved, they stopped and recorded the result. The maximum number of attempts was limited to ten.

Also, participants completed a post-training questionnaire based on a Likert scale to access the perceived feasibility and educational value of the simulator, the anatomical realism of landmarks and radiographic realism with scores: strongly agree (5), agree (4), neutral (3), disagree (2), strongly disagree (1) [13].

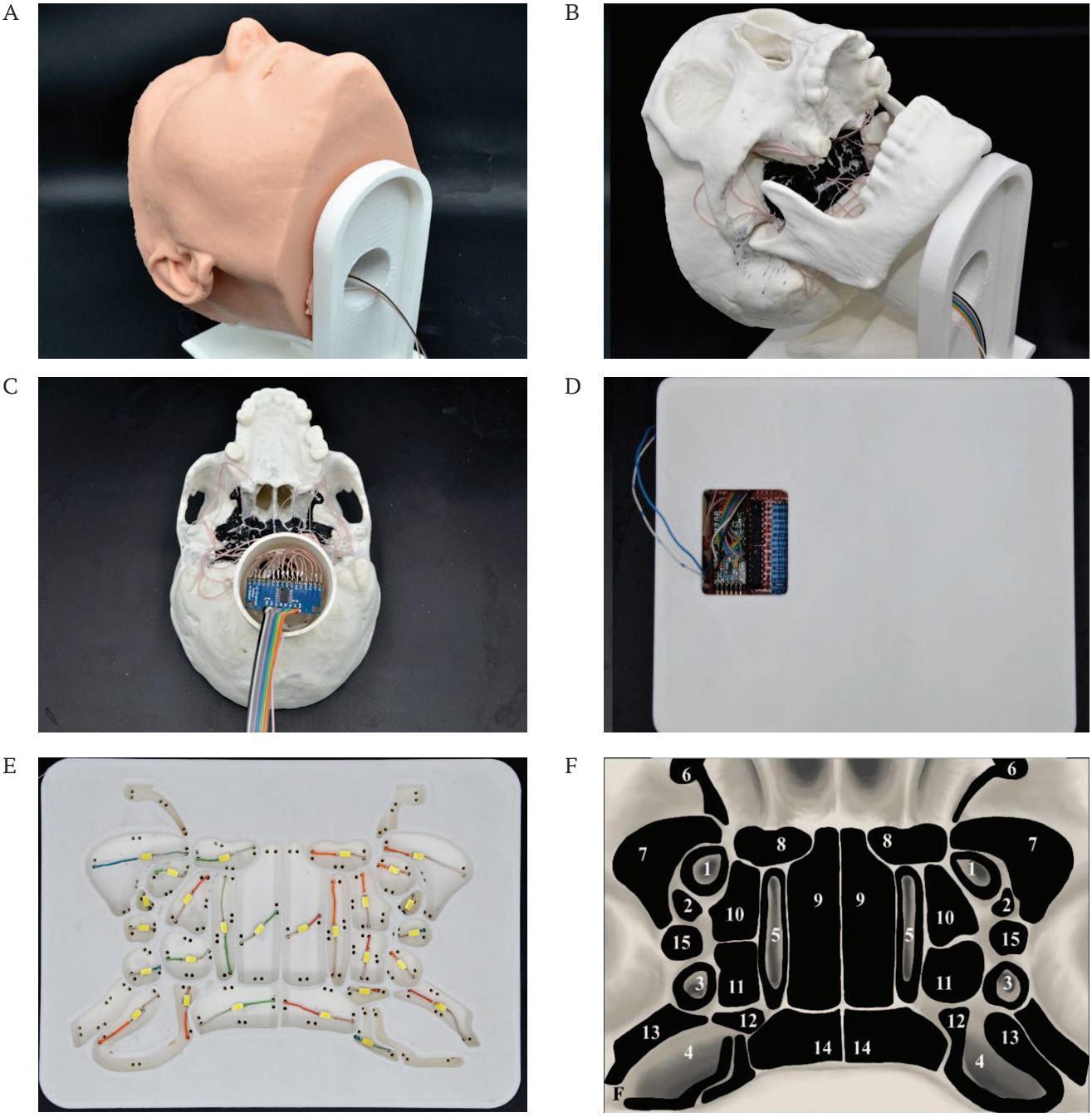

FIG. 2. The electronic part of the 3D head model for practicing foramen ovale puncture.
A. The silicone 3D head model with electronics unit.
B. The 3D printed head model with electroactive zones printed with black U3 Flex Conductive filament.
C. The electronics block of a 3D skull model based on ARDUINO microcontroller.
D. The electronics block of the LED screen based on ARDUINO microcontroller.
E. The LED screen.
F. The scheme of the LED screen: 1 – foramen ovale, 2 – foramen spinosum, 3 – external opening of the carotid canal, 4 – foramen jugulare, 5 – foramen lacerum, 6 – inferior orbital fissure, 7–14 – adjacent non-contact zones.

Statistical analysis

Descriptive statistics were reported as absolute frequencies and percentages for categorical variables, and as medians with interquartile ranges (25^{th}; 75^{th} percentile) for ordinal or non-normally distributed continuous variables. For normally distributed continuous variables, data were expressed as mean with standard deviation. Normality was assessed with the Shapiro–Wilk test and verified visually using Q–Q plots and histograms.

The median values were calculated from multiple puncture attempts performed by each participant within each training phase, and then group medians

with interquartile ranges were determined across all participants in each group. Between-group comparisons were performed with a two-tailed independent Student's *t*-test for normally distributed data or the Mann–Whitney *U*-test for non-normally distributed data. Comparisons of paired data before and after training were performed using the paired Student's *t*-test for normally distributed differences or the Wilcoxon signed-rank test for non-normally distributed differences. Five-level Likert responses were compared between groups with the two-sided Fisher–Freeman-Halton exact test (5×2 contingency tables). For sensitivity analysis, Likert scores were dichotomized (⩾ "Agree" vs. ⩽ "Neutral"), and a two-sided Fisher's exact test (2×2) was applied. All tests were two-tailed, and a p-value < 0.05 was considered statistically significant. Statistical analyses were conducted in R version 4.5.1 (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Analysis of puncture performance before and after training revealed statistically significant improvement across all evaluated parameters in both groups (Table). Following the training, puncture time was reduced by approximately half in both groups. The number of puncture attempts before the first successful, complication-free attempt was reduced by 50% in the physicians' group and by 60.3% in the residents' group.

The total number of complications after training decreased by 57.8% in the physicians' group and by 59.0% in the residents' group. Initial complication rates associated with inferior orbital fissure damage, jugular foramen puncture and puncture of external opening of the carotid canal were higher in the residents' group. While initial frequency of other complications (foramen lacerum puncture, puncture of the first branch of the trigeminal nerve, puncture of the internal carotid artery and foramen spinosum puncture) was low and similar both in physicians' and residents' groups (Table).

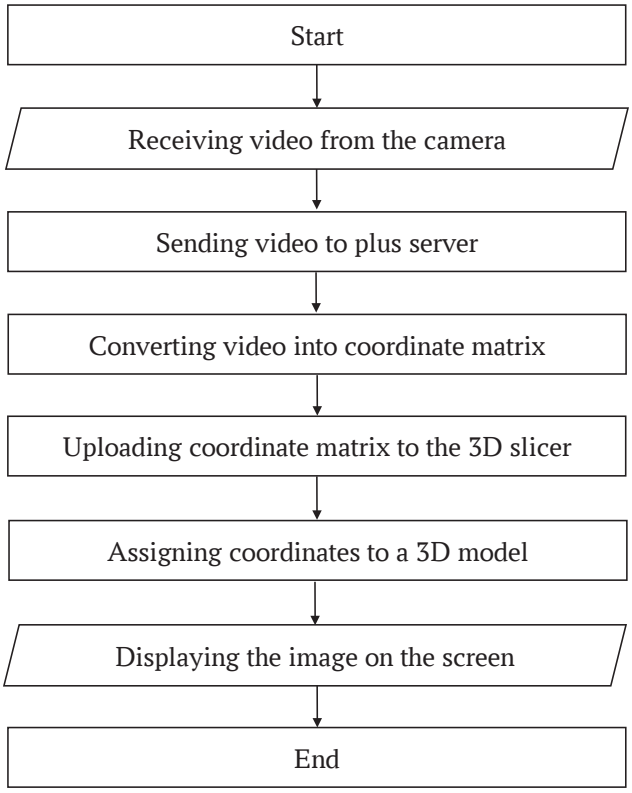

FIG. 3. The block diagram of computer vision technology.

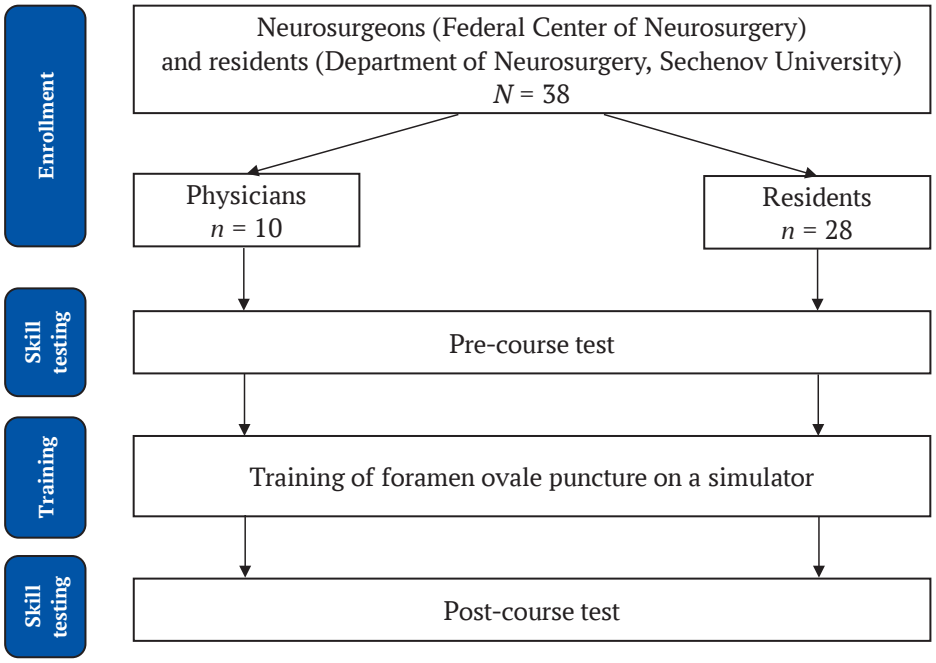

FIG. 4. Study flowchart.

Table. **Puncture results before and after training**

Parameter	Physicians (*n* = 10)		*p* value	Residents (*n* = 28)		*p* value
	Before	After		Before	After	
Puncture time, s	186.0 ± 77.2	90.0 ± 51.0	<0.001	527.1 ± 135.0[b]	237.9 ± 82.4[b]	<0.001
Attempts to puncture the foramen ovale, *n*	2.8 ± 0.8	1.4 ± 0.5	<0.001	6.6 ± 2.1[b]	2.6 ± 1.0[b]	<0.001
Total number of complications, *n*	4.5 ± 1.6	1.9 ± 0.7	<0.001	9.5 ± 3.3[b]	3.9 ± 1.7[b]	<0.001
Complications associated with:						
inferior orbital fissure damage, *n*	0.5 (0; 1.75)	0 (0; 0)	n.s.	2 (0.75; 3)[a]	1 (1; 2)[b]	<0.05
jugular foramen puncture, *n*	1 (0.25; 1)	0 (0; 1)	n.s.	3 (2; 4)[b]	1 (1; 2)[b]	<0.001
external opening of the carotid canal puncture, *n*	1 (0.25; 1)	0 (0; 0)	<0.05	2 (1; 3)[a]	0 (0; 0)	<0.001
foramen lacerum puncture, *n*	0.5 (0; 1)	0 (0; 1)	n.s.	1 (0; 2)	0 (0; 1)	<0.001
foramen spinosum puncture, *n*	0 (0; 0)	0 (0; 0)	n.s.	0 (0; 1)	0 (0; 0.25)	n.s.
puncture of the first branch of the trigeminal nerve, *n*	0.5 (0; 1)	0 (0; 0.75)	n.s.	0 (0; 1)	0 (0; 0.25)	n.s.
internal carotid artery puncture, *n*	0 (0; 1)	0 (0; 0.75)	n.s.	0 (0; 1)	0 (0; 0)	n.s.

Notes: [a] $p < 0.05$, [b] $p < 0.001$ when compared to a group of physicians at the same point of the study.
n.s. – not significant.

Following training, the complication rate related to puncture of the external opening of the carotid canal decreased by 88.9% in physicians and by 94.9% in residents, resulting in no statistically significant difference between the two groups post-training (Table). Complications related to puncture of the inferior orbital fissure and jugular foramen decreased by 75.0% and 50.0%, respectively, in physicians, and by 35.3% and 51.9%, respectively, in residents; however, the rates among residents remained significantly higher compared to those of physicians. Other puncture-related complications decreased as follows: foramen lacerum – by 42.9% in physicians and 68.4% in residents; foramen spinosum – by 0% and 44.4%, respectively; first branch of the trigeminal nerve – by 50.0% and 27.3%; internal carotid artery – by 40.0% and 50.0%. Post-training complication rates for these structures were comparable between physicians and residents.

The feasibility and construct validity of the simulator was confirmed by the Likert scale. Both groups rated the simulator as "useful for educational purposes" and "realistic" from anatomical and radiographic points of view.

The perceived feasibility and educational value of the simulator, the anatomical realism of landmarks and radiographic realism, assessed by the Likert scale, received equivalent ratings from both the physicians' group and the residents' group (Fig. 5).

DISCUSSION

Various puncture-based interventions for trigeminal neuralgia share a common technical approach: accessing the GG via FO puncture [14]. Despite the technical simplicity of performing FO puncture, the lack of surgical skills may lead to serious complications [15].

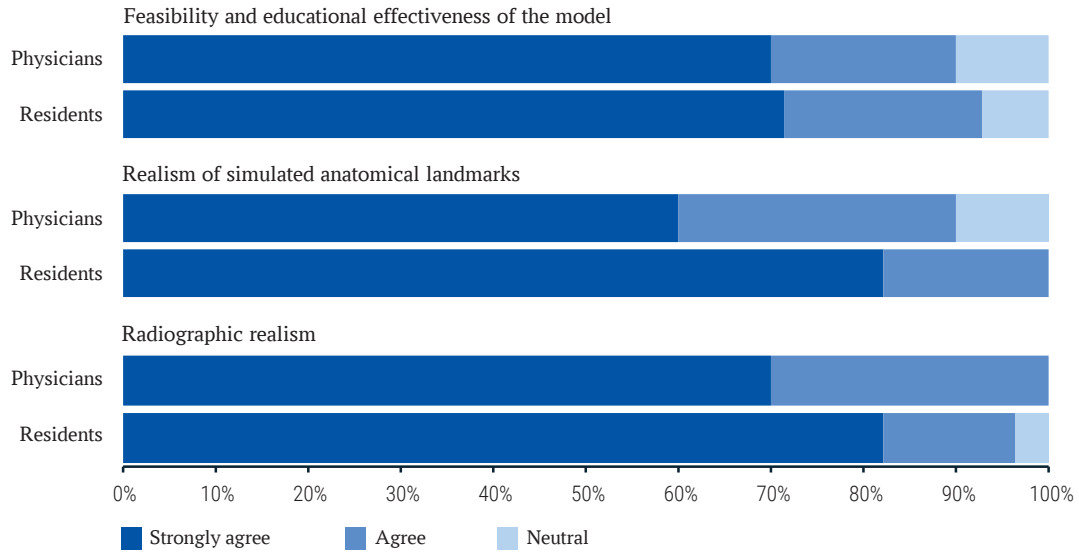

FIG. 5. The training results according to the Likert scale.

The iatrogenic nature of such complications is most frequently attributed to the surgeon's insufficient competence, leading to anatomical disorientation and difficulty maneuvering the puncture needle under fluoroscopic control, primarily due to inadequate hand-eye coordination [10]. To improve a surgeon's competence in puncture-based interventions, it is necessary to provide quality preoperative training in a safe environment [16].

The present study demonstrated the effectiveness of integrating engineering technology and AI in creating a 3D simulator for teaching FO puncture in the treatment of trigeminal neuralgia. The high Likert scale scores for the educational effectiveness of the simulator (70.0–71.4% of participants selected the maximum score), realistic anatomical landmarks (60.0–82.1%) and radiological visualization (70.0–82.1%) confirm the high quality of the developed model. The results of this study showed a statistically significant improvement in all evaluated parameters in both groups of participants after training on the developed model.

The most encouraging result was a 50% reduction in intervention time in both groups after simulation training despite a significant difference in pre-training scores (difference between physicians and residents 341.1 sec), indicating the development of sustainable practical skills regardless of the participants' initial training level. Equally important, a reduction in the number of puncture attempts by 50% in physicians and 60.3% in residents indicates improved accuracy in performing the procedure. The more pronounced improvement in the resident group may be due to the greater potential for skill development in less experienced professionals, consistent with the concept of a learning curve in surgery [17, 18].

The results of this study showed a significant reduction in the total number of complications (around 60% in both groups), which is a key indicator of the clinical relevance of the developed simulator. A more detailed analysis of the types of complications showed that the greatest improvement was observed for puncture of the foramen jugulare, inferior orbital fissure and external carotid orifice in the resident group. Notably, the initially higher complication rates in the resident group approached those of experienced physicians for most parameters after training. The exceptions were puncture of the first branch of the trigeminal nerve and internal carotid artery, where differences between groups were minimal both before and after training. This observation indicates the formation of hand-eye coordination skills and a more accurate understanding of the trajectory of the puncture needle in the areas of the skull base. Formation of the skill of hand-eye coordination in performing various types of surgical interventions has received much attention in the literature [6, 19–21]. The 3D model developed in this study accurately reproduces the anatomical location of the FO, functionally significant areas of the skull base, GG and internal carotid artery. Moreover, the use of electrically conductive carbon nanotube materials to create feedback zones provides immediate tactile and visual confirmation of contact with critical anatomical structures, which helps prevent the formation of incorrect motor skills and improves the overall quality of learning.

Training of hand-eye coordination for FO puncture usually requires fluoroscopic guidance with a C-arc, which limits training time due to the negative effects of ionizing radiation [22]. Integrating computer vision into the training of FO puncture on a 3D printed model in our study provides a safe and effective alternative [23–25]. In this study, we developed a computer vision algorithm to detect a QR code attached to the puncture needle, thereby mimicking the functionality of the C-arm and enabling the acquisition of hand-eye coordination skills during FO puncture. Using QR code to track the instrument and creating a virtual environment in the 3D Slicer provides a safe alternative to fluoroscopic guidance, which is especially important for repeated training sessions. Another significant advantage of the developed system is its dependence on standard equipment (webcam and personal computer with graphics processor), which makes it affordable for wide implementation in training centers. The elimination of expensive X-ray equipment significantly reduces the overall cost of training, which opens up opportunities for scalable training.

Excluding the cost of a 3D printer, the cost of creating a simulator is significantly lower than the cost of purchasing and storing cadaver material. For instance, the price of a single cadaveric human head is between $600 and $1000 in the US, Russia and Italy [26–28]. Despite the fact that cadaveric material is the most suitable for training, access to cadaveric heads is limited by thanks to legal and financial restrictions [29]. In addition, the costs of maintaining anatomical laboratories are very high and the establishment of a cadaveric laboratory requires the resolution of a number of issues regarding its location, the acquisition of instruments, the purchase, storage and disposal of cadaveric material, as well as strict inter-institutional co-operation to resolve legislative aspects, which limits the use of this material in the modern educational process [30, 31].

Limitations of the study and further research perspectives

The study had a limited sample size (38 participants), which may reduce the statistical significance of the results and their generalizability to a wider population of learners. The model is based on data from a single patient with trigeminal neuralgia, which does not take into account anatomical variations between different patients and may limit the realism of the training process.

Further development of this topic could include the creation of a library of 3D models based on different anatomical variants of the FO to increase the versatility

of the simulator, as well as multicenter randomized controlled trials to assess the impact of simulation training on clinical outcomes and patient safety in real-world practice.

CONCLUSION

The conducted study emphasizes the effective integration of engineering technology and AI as a useful and safe tool for teaching puncture-based treatment of trigeminal neuralgia. The results of the study demonstrate that the developed 3D head simulation model is highly realistic and educationally valuable, supported by both quantitative outcomes and qualitative assessments. Procedure time was significantly reduced, the number of puncture attempts decreased, and the incidence of complications involving damage to anatomical structures was lowered. The use of available equipment and open source software solutions makes this technology scalable for widespread implementation in educational institutions, which can significantly improve the quality of neurosurgeon training and, ultimately, patient safety.

AUTHORS CONTRIBUTIONS

Albert A. Sufianov, Rinat A. Sufianov and Nargiza A. Garifullina developed the idea for the research and its design. Albert A. Sufianov, Nargiza A. Garifullina and Margarita F. Chakhmakhcheva performed the scientific literature search and collected the primary data. Aleksandr N. Zyryanov and Anton D. Zakshauskas developed the 3D model and neuronavigation system. Albert A. Sufianov, Rinat A. Sufianov, Nargiza A. Garifullina and Margarita F. Chakhmakhcheva participated in the writing and editing of the manuscript. All authors approved the final version of the article.

ВКЛАД АВТОРОВ

А.А. Суфианов, Р.А. Суфианов и Н.А. Гарифуллина разработали основную концепцию и дизайн исследования. А.А. Суфианов, Н.А. Гарифуллина и М.Ф. Чахмахчева выполнили научный поиск литературы и сбор первичных данных. А.Н. Зырянов и А.Д. Закшаускас разработали 3D-модель и систему нейронавигации. А.А. Суфианов, Р.А. Суфианов, Н.А. Гарифуллина и М.Ф. Чахмахчева принимали участие в написании основного текста и редактуре статьи. Все авторы утвердили окончательную версию публикации.

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ИНФОРМАЦИЯ ОБ АВТОРАХ / INFORMATION ABOUT THE AUTHORS

Rinat A. Sufianov✉**,** Cand. of Sci. (Medicine), Associate Professor, Department of Neurosurgery, Sechenov First Moscow State Medical University (Sechenov University); neurosurgeon, Department of Neurooncology, N.N. Blokhin National Medical Research Center of Oncology.
ORCID: https://orcid.org/0000-0003-4031-0540

Суфианов Ринат Альбертович✉**,** канд. мед. наук, доцент кафедры нейрохирургии ФГАОУ ВО «Первый МГМУ им. И.М. Сеченова» Минздрава России (Сеченовский Университет); врач-нейрохирург отделения нейроонкологии ФГБУ «НМИЦ онкологии им. Н.Н. Блохина» Минздрава России.
ORCID: https://orcid.org/0000-0003-4031-0540

Nargiza A. Garifullina, postgraduate student, Department of Neurosurgery, Sechenov First Moscow State Medical University (Sechenov University); neurosurgeon, Department of Admissions and Advisory, Federal Center of Neurosurgery (Tyumen); Assistant Professor, Department of Pharmacology, Tyumen State Medical University.
ORCID: https://orcid.org/0000-0001-6918-5339

Гарифуллина Наргиза Аскатовна, аспирант кафедры нейрохирургии ФГАОУ ВО «Первый МГМУ им. И.М. Сеченова» Минздрава России (Сеченовский Университет); врач-нейрохирург приемо-консультативного отделения ФГБУ «Федеральный центр нейрохирургии» Минздрава России (г. Тюмень); ассистент кафедры фармакологии ФГБОУ ВО «Тюменский ГМУ» Минздрава России.
ORCID: https://orcid.org/0000-0001-6918-5339

Aleksandr N. Zyryanov, engineer, Federal Center of Neurosurgery (Tyumen).
ORCID: https://orcid.org/0009-0004-2874-2302

Зырянов Александр Николаевич, инженер ФГБУ «Федеральный центр нейрохирургии» Минздрава России (г. Тюмень).
ORCID: https://orcid.org/0009-0004-2874-2302

Anton D. Zakshauskas, engineer, Federal Center of Neurosurgery (Tyumen).
ORCID: https://orcid.org/0009-0008-1485-1574

Закшаускас Антон Данилович, инженер ФГБУ «Федеральный центр нейрохирургии» Минздрава России (г. Тюмень).
ORCID: https://orcid.org/0009-0008-1485-1574

Margarita F. Chakhmakhcheva, student, Institute of Motherhood and Childhood, Tyumen State Medical University.
ORCID: https://orcid.org/0009-0009-1924-7998

Albert A. Sufianov, Dr. of Sci. (Medicine), Professor, Corresponding Member of the RAS, Head of the Department of Neurosurgery, Sechenov First Moscow State Medical University (Sechenov University); Chief Physician, Federal Center of Neurosurgery (Tyumen); Director, Educational and Research Institute of Neurosurgery, Peoples' Friendship University of Russia; Professor, Department of Neurosurgery, King Edward Medical University.
ORCID: https://orcid.org/0000-0001-7580-0385

Чахмахчева Маргарита Фотиевна, студентка Института материнства и детства ФГБОУ ВО «Тюменский ГМУ» Минздрава России.
ORCID: https://orcid.org/0009-0009-1924-7998

Суфианов Альберт Акрамович, д-р мед. наук, профессор, член-корреспондент РАН, заведующий кафедрой нейрохирургии ФГАОУ ВО «Первый МГМУ им. И.М. Сеченова» Минздрава России (Сеченовский Университет); главный врач ФГБУ «Федеральный центр нейрохирургии» Минздрава России (г. Тюмень); директор Учебно-научного института нейрохирургии ФГАОУ ВО «РУДН им. Патриса Лумумбы»; профессор кафедры нейрохирургии Медицинского университета короля Эдуарда.
ORCID: https://orcid.org/0000-0001-7580-0385

✉ Corresponding author / Автор, ответственный за переписку

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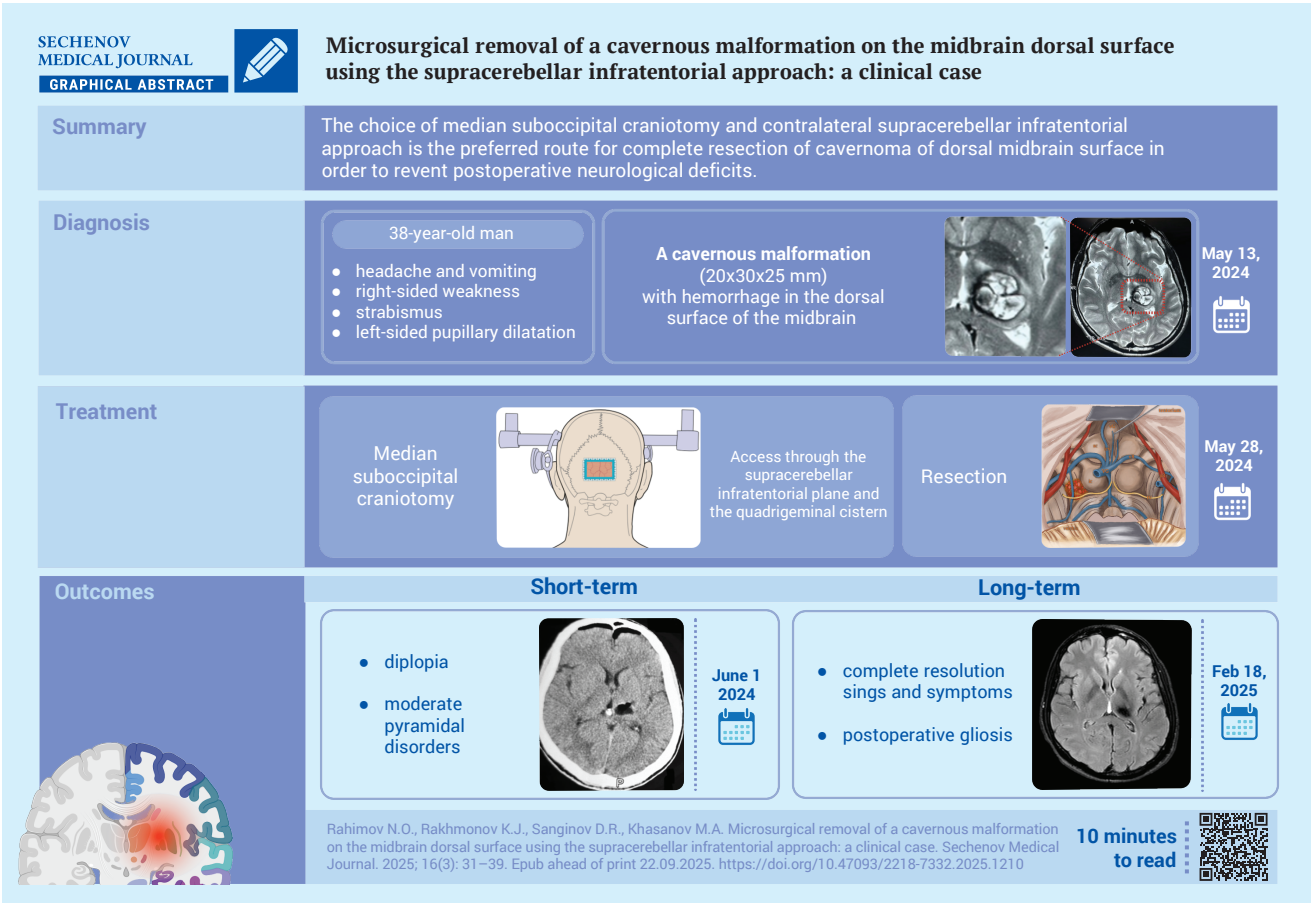
Microsurgical removal of a cavernous malformation on the midbrain dorsal surface using the supracerebellar infratentorial approach: a clinical case

Narzullo O. Rahimov[1,2,✉], Khurshed J. Rakhmonov[1,2], Dzhumaboy R. Sanginov[1], Mahmarajab A. Khasanov[1]

[1]Avicenna Tajik State Medical University
29–31, Sino Ave., Sino str., Dushanbe, 734003, Republic of Tajikistan
[2]SI National Medical Center of Republic of Tajikistan "Shifobakhsh"
59, I. Somoni Ave., Dushanbe, 734026, Republic of Tajikistan



Abstract

Common surgical approaches to the dorsal midbrain include: the occipital transtentorial, supracerebellar infratentorial, posterior subtemporal, and the tonsilloveal transaqueductal approaches.

Case report. A 38-year-old man presented with mild right-sided weakness and diplopia following an episode of headache and vomiting two weeks prior to admission. A neurological examination revealed mild right-sided weakness, a downward and outward strabismus, a mild left ocular mydriasis and accommodation paralysis alongside alternating syndrome. Magnetic resonance imaging revealed a 20×30×25 mm rupture of the cavernous malformation of the left midbrain peduncle as well as hematomas within the cavernoma. Using the supracerebellar infratentorial approach in a sitting position with minimal incision of dorsal midbrain, the cavernoma was completely resected together with

surrounding subacute hematoma. In the early postoperative period, a regression of neurological symptoms was observed.
Discussion. The choice of median suboccipital craniotomy and contralateral supracerebellar infratentorial approach is the preferred route for complete resection of cavernoma of dorsal midbrain surface in order to avoid any postoperative neurological deficit.

Keywords: cavernoma; lesion of the midbrain peduncles; access to the dorsal part of the midbrain; hematoma; removal of midbrain formations
MeSH terms:
CASE REPORTS
CENTRAL NERVOUS SYSTEM VASCULAR MALFORMATIONS – DIAGNOSTIC IMAGING
CENTRAL NERVOUS SYSTEM VASCULAR MALFORMATIONS – SURGERY
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MICROSURGERY – METHODS
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CONTACT INFORMATION:
Narzullo O. Rahimov, Cand. of Sci. (Medicine), Associate Professor, Department of neurosurgery and combined trauma, Avicenna Tajik State Medical University; neurosurgeon, SI National Medical Center of Republic of Tajikistan "Shifobakhsh".
Address: 59, I. Somoni Ave., Dushanbe, 734026, Republic of Tajikistan
E-mail: narzullorahimov91@gmail.com

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Микрохирургическое удаление кавернозной мальформации дорсальной поверхности среднего мозга путем супрацеребеллярного инфратенториального доступа: клинический случай

Н.О. Рахимов[1,2,✉], Х.Д. Рахмонов[1,2], Д.Р. Сангинов[1], М.А. Хасанов[1]
[1]ГОУ «Таджикский государственный медицинский университет имени Абуали ибни Сино»
пр-т Сино, ул. Сино, д. 29–31, г. Душанбе, 734003, Республика Таджикистан
[2]ГУ «Национальный медицинский центр Республики Таджикистан Шифобахш»
пр-т И. Сомони, д. 59, г. Душанбе, 734026, Республика Таджикистан

Аннотация

Известные хирургические доступы к дорсальной части среднего мозга включают: затылочный транстенториальный, супрацеребеллярный инфратенториальный, задний субтемпоральный и тонзиллоувеальный трансакведуктальный подходы.

Описание случая. 38-летний мужчина обратился с жалобами на легкую правостороннюю слабость и диплопию после эпизода головной боли и рвоты за две недели до поступления. В неврологическом статусе выявлено незначительное снижение мышечной силы с правой стороны, косоглазие вниз и наружу, легкий мидриаз и паралич аккомодации левого глаза, альтернирующий синдром. С помощью магнитно-резонансной томографии выявлен разрыв кавернозной мальформации размером 20×30×25 мм левой ножки среднего мозга, гематомы в каверноме. Путем супрацеребеллярного инфратенториального доступа в положении сидя с минимальным разрезом дорсальной части среднего мозга кавернома была полностью резецирована вместе с окружающей подострой гематомой. В раннем послеоперационном периоде наблюдался регресс неврологической симптоматики.
Обсуждение. Выбор медианной субокципитальной краниотомии и контралатерального супрацеребеллярного инфратенториального доступа является предпочтительным для полной резекции кавернома дорсальной поверхности среднего мозга во избежание послеоперационного неврологического дефицита.

Ключевые слова: кавернома; поражение ножек среднего мозга; доступ к дорсальной части среднего мозга; гематома; удаление образований среднего мозга
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НЕРВНОЙ СИСТЕМЫ ЦЕНТРАЛЬНОЙ СОСУДИСТЫЕ МАЛЬФОРМАЦИИ – ХИРУРГИЯ
МОЗГ СРЕДНИЙ – КРОВОСНАБЖЕНИЕ
МОЗГ СРЕДНИЙ – ХИРУРГИЯ
МИКРОХИРУРГИЯ – МЕТОДЫ
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КОНТАКТНАЯ ИНФОРМАЦИЯ:
Рахимов Нарзулло Одинаевич, кандидат медицинских наук, доцент кафедры нейрохирургии и сочетанной травмы ГОУ «ТГМУ им. Абуали ибни Сино»; врач-нейрохирург ГУ «Национальный медицинский центр Республики Таджикистан Шифобахш»
Адрес: пр-т И. Сомони, д. 59, г. Душанбе, 734026, Республика Таджикистан
E-mail: narzullorahimov91@gmail.com

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Abbreviations:
CM – cavernous malformation
CT – computed tomography
MRI – magnetic resonance imaging

Cavernous malformations (CM) or cavernomas of the central nervous system are formations consisting of multiple adjacent cavities of irregular shape (caverns), lined with endothelium and filled with blood.

According to magnetic resonance imaging (MRI) data at the screening stage and several thousand autopsies, CM of the central nervous system is detected in 0.3–0.6% of the population [1, 2]. Most often, the first symptoms appear at a young age – on average, at 23 years [3].

Of all CMs of the brain, localization in the brainstem accounts for 19 to 30% [3], of which 14.2–25% occur in the midbrain [4]. In cerebral CMs, the annual frequency

of primary hemorrhages is 0.39-1.3%, recurrent – 4.5–22.9% [5]. It is believed that brain cavernomas located in the brainstem area are most prone to recurrent hemorrhages with an annual risk ranging from 21–60% and complications during surgical intervention than with other localizations of cavernomas [6–9]. The risk of recurrent bleeding increases with incomplete surgical resection [9, 10]. These features allow to distinguish brainstem CMs into a separate group.

The tactics of surgical treatment of primary bleeding from the midbrain CM depend on the timing of the hemorrhage, age and somatic status of the patient and necessitate an individual approach to developing an optimal treatment strategy.

The purpose of this case report is to demonstrate the experience of successful radical resection of the midbrain peduncle CM by the supracerebellar infratentorial approach as an effective surgical strategy for primary hemorrhage in a young patient.

CASE REPORT

A 38-year-old man, a builder, sought medical help at the SI "National Medical Center of the Republic of Tajikistan Shifobakhsh" on May 13, 2024 with complaints of diplopia and mild weakness in the right limbs, which arose suddenly after an episode of headache and vomiting about two weeks previously.

Clinical examination on admission: clear consciousness, 15 points according to the Glasgow Coma Scale, somatic status without any peculiarities: respiratory rate 16 per minute, heart rate 80 per minute, blood pressure 120/80 mm Hg. In the neurological status, a slight decrease in strength on the right side was noted – IV/V degree according to the classification of muscle tone study[1], strabismus downward and outward, mild mydriasis and paralysis of accommodation of the left eye alongside alternating syndrome.

Computed tomography (CT) of the brain revealed a poorly defined hyperdense formation in the lower part of the dorsal surface of the left peduncle of the midbrain measuring 20x30x25 mm. MRI of the brain revealed a hyperintense lesion in T1- and T2-weighted images with a clearly defined hypointense rim, hematomas in a cavernoma of 20×30×25 mm (Fig. 1A–C).

Based on clinical data and neuroimaging results, the following diagnosis was made: rupture of CM of the left midbrain peduncle, hematomas in the cavernoma.

To avoid any postoperative neurological deficit (as assessed by additional scales: 4 points on the Spetzler–Martin [11] and 3 points on the Lawton–Young [12]), a median suboccipital craniotomy with a contralateral supracerebellar infratentorial approach was chosen for radical cavernoma resection (Fig. 2A–E).

Surgery Procedure

The operation was performed on May 28, 2024 under general endotracheal anesthesia with the patient in a sitting position – to give the back a vertical position, and with the head tilted forward to smooth the angle of the tentorium. The patient's head was rigidly fixed using a Mayfield-Keys clamp. The Carl Zeiss OPMI Vario S88 operating microscope (Carl Zeiss, Germany) was used during the operation.

Surgical access was achieved through a 12 cm long linear skin incision in the parietal-occipital region. A burr hole was created in the occipital protuberance region,

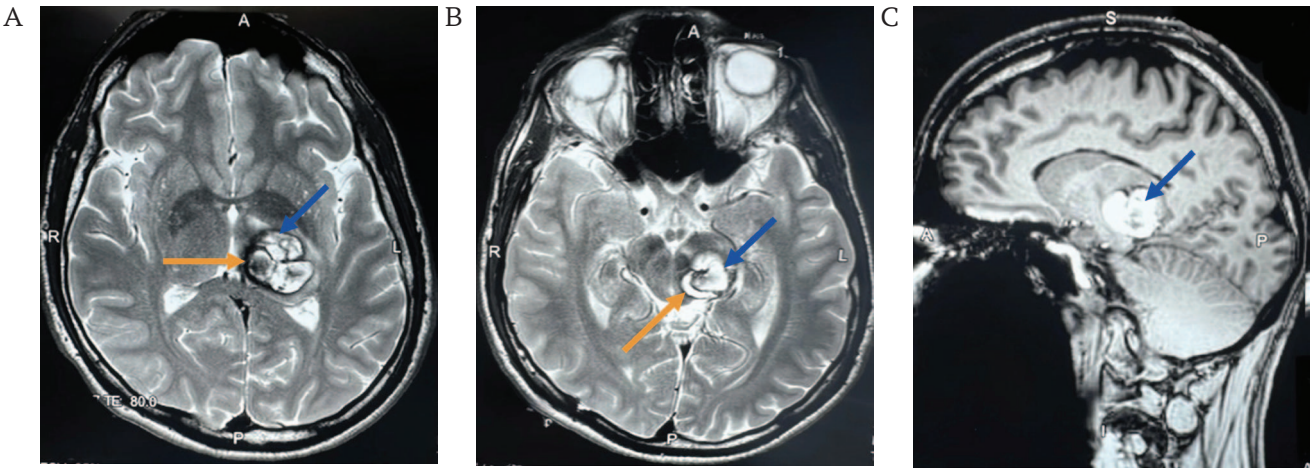


FIG. 1. Magnetic resonance imaging of a 38-year-old patient with a cavernous malformation measuring 20×30×25 mm in the dorsal part of the left peduncle of the midbrain (May 13, 2024).
A, B. Axial sections, T2-weighted image: cavernous malformation (blue arrow), hematomas in the cavernoma (orange arrow).
C. Sagittal section, T1-weighted image: cavernous malformation (arrow).

[1] Index of Clinical Guidelines by the Russian Ministry of Health / Clinical Guidelines / Mononeuropathies (Approved by the Ministry of Health of the Russian Federation) https://cr.minzdrav.gov.ru/preview-cr/166_2 (access date: 13.05.2024).

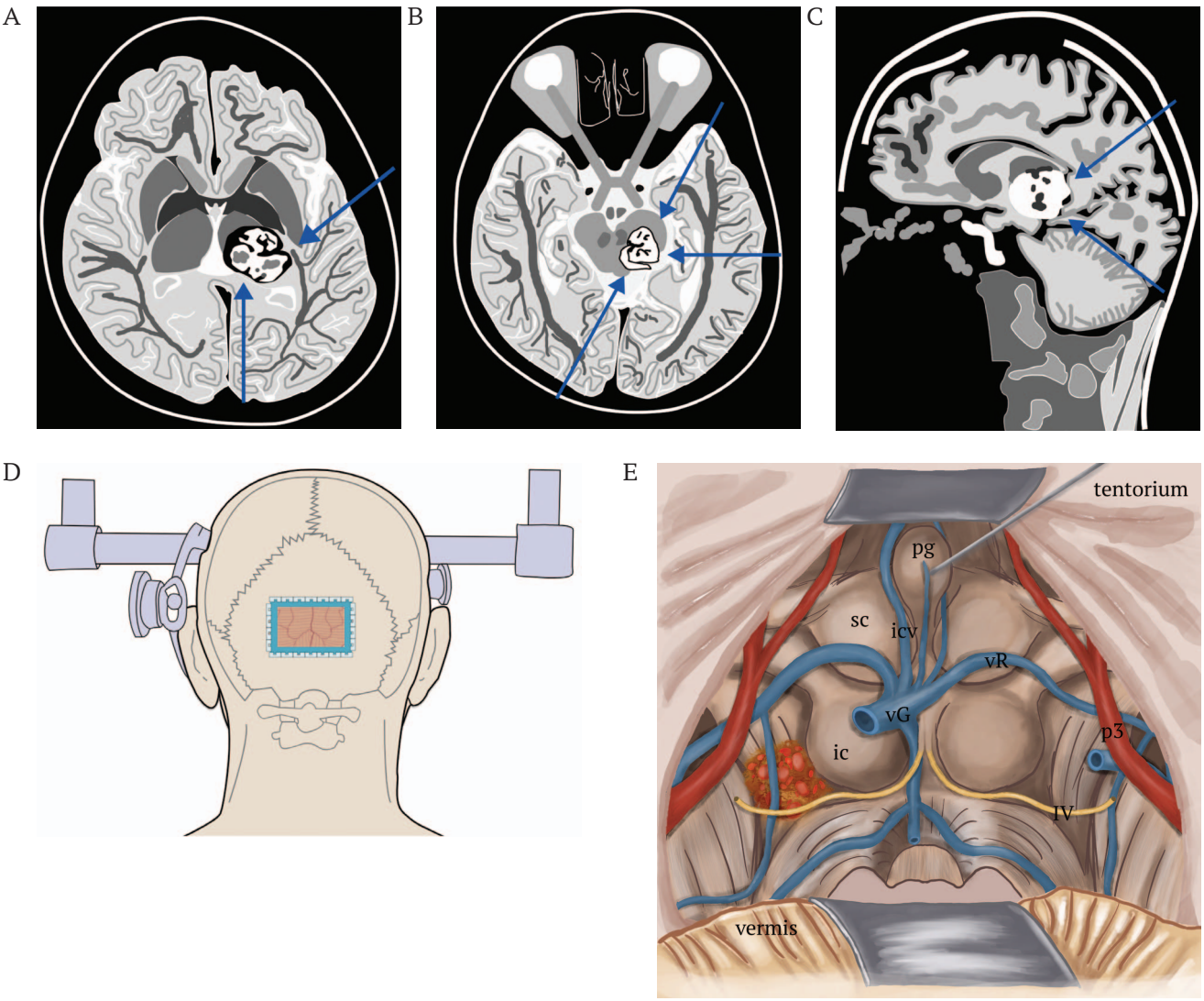


FIG. 2. Schematic representation of the localization of the cavernoma of the dorsal surface of the midbrain and the choice of strategy for its resection.
A. Axial section. The arrows indicate the approaches to the midbrain: left lower – supracerebellar infratentorial; right upper – posterior subtemporal.
B. Axial section. The arrows indicate the approaches to the midbrain: left lower – contralateral supracerebellar infratentorial; right upper – anterior subtemporal; right lower – posterior subtemporal approaches.
C. Sagittal section. The arrows indicate the approaches to the midbrain: right upper – occipital transtentorial; right lower – supracerebellar infratentorial.
D. Exposure of the cavernoma using torcular craniotomy and supracerebellar infratentorial approach (blue line).
E. Access to the cavernoma through the supracerebellar infratentorial plane and the quadrigeminal cistern; identification of the ascending deep cerebral veins; determination of the feeding arteries of the pons and midbrain; review of the lateral sections; dissection of the quadrigeminal cistern to provide a free corridor (superior view of the midbrain, pons, tentorium from the pineal region and superior cerebellar peduncle); mobilization of the vessels and veins draining into the superior sagittal sinus.

Note: ic – inferior colliculus; icv – internal cerebral vein; pg – pineal gland; p3 – posterior cerebral artery (segment p3); sc – superior colliculus; vG – vein of Galen; vR – vein of Rosenthal; IV – cranial nerves (IV pair).

which provided a circular craniotomy measuring 80x60 mm with exposure of the sinus drain and contralateral supracerebellar infratentorial access with gravitational retraction of the cerebellum. The upper edge of the bone flap was located on the transverse sinus.

A semi-oval incision of the dura mater, reinforced with interrupted sutures, was made, which elevated the transverse sinuses and provided entry into the supracerebellar infratentorial plane. The sagging of the cerebellum widened the natural corridor to the

quadrigeminal cistern. Cerebrospinal fluid was drained from the cisterna magna, and the cerebellum was retracted by dissection of the arachnoid adhesions connecting the posterior superior border of the cerebellum to the outer edge of the tentorium. To access the free edge of the tentorium, the bridging veins between the cerebellum and the tentorium were divided. The arachnoid membrane dissection of the posterior edge of the quadrigeminal cistern was performed to visualize the dorsal part of the midbrain.

The supracerebellar infratentorial approach in the sitting position opens the anatomical plane so widely that dissection is significantly facilitated. Any discomfort from working with raised arms is compensated by the panorama without a retractor and the operative field cleared by gravity (Fig. 3A). Arachnoid dissection was performed, and large deep veins (V. Galen, internal cerebral veins, internal occipital veins, basal veins of Rosenthal, pericentral veins of the cerebellum) were identified. The contralateral approach allowed visualization of the IV pair of cranial nerves and the P3 segment of the posterior cerebral artery.

With a minimal incision in the dorsal part of the midbrain (Fig. 3B), the cavernoma was completely resected together with the surrounding subacute hematoma measuring 2×3×2.5 cm (Fig. 3C). Hemostasis was achieved until the lavage water was clear. A hemostatic collagen sponge was placed in the cavernoma bed. The dura mater was sutured hermetically. The bone flap was fixed with threads. Layer-by-layer suturing of the wound was performed. An aseptic dressing was applied. The total blood loss was 250 ml.

A control CT scan in the postoperative period was performed on the third day; according to the study data, the condition after median suboccipital craniotomy, residual cavernoma, and repeated hemorrhage were not detected (Fig. 4A, B).

In the postoperative period, the patient's consciousness is clear (15 points on the Glasgow Coma Scale), diplopia and moderate pyramidal disorders disappeared on the 12th day. The course of the postoperative period is smooth, without the development of postoperative complications. The patient was discharged from the hospital on the 15th day after the surgical intervention.

The patient came for a follow-up examination and assessment of the long-term treatment results on February 18, 2025. During the examination, the patient's consciousness was clear. No sensory or motor disturbances were observed after the surgery. He was able to walk and take care of himself independently. The patient has fully recovered and returned to professional activities without any restrictions.

A MRI of the brain was undertaken on February 18, 2025, and here we can observe the brain's condition after removal of the cavernoma. The MR showed signs of postoperative gliosis changes. No residual cavernoma or recurrent hemorrhage was detected (Fig. 5A, B).

DISCUSSION

At present, one of the main issues in treating midbrain CM is determining the timing of the surgical intervention, be it in the acute or the subacute period.

In our case, the patient was operated on the 20th day after the primary hemorrhage. The cavernoma was located in the subacute hematoma, which made it easy to remove together with the cavernoma itself.

According to generally accepted practice and in line with our clinical experience, surgical treatment in the subacute stage of hemorrhage, when the hematoma is liquefied, is effective for maximum removal of the hematoma with minimal incision of the brainstem [13]. In such cases, a limited incision of the brainstem contributes to the most complete neurological recovery.

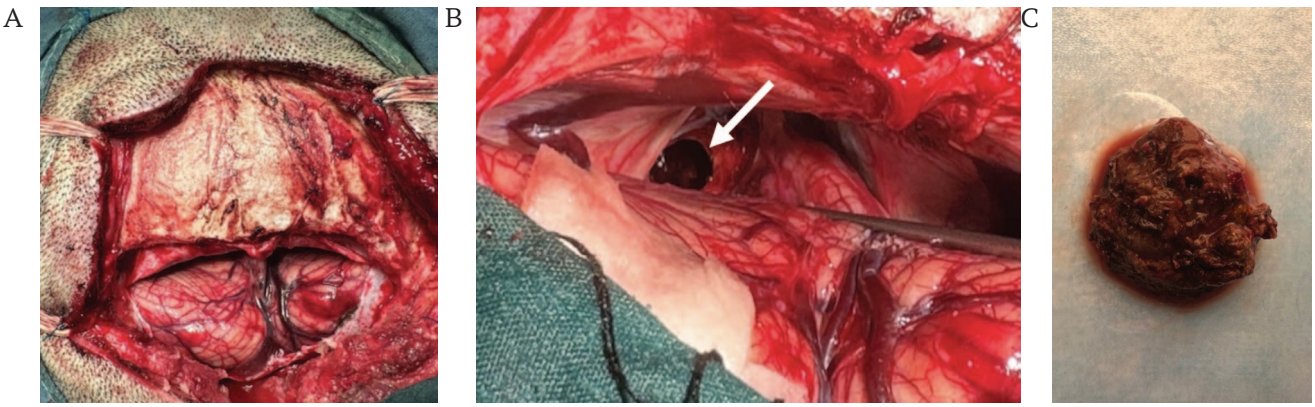
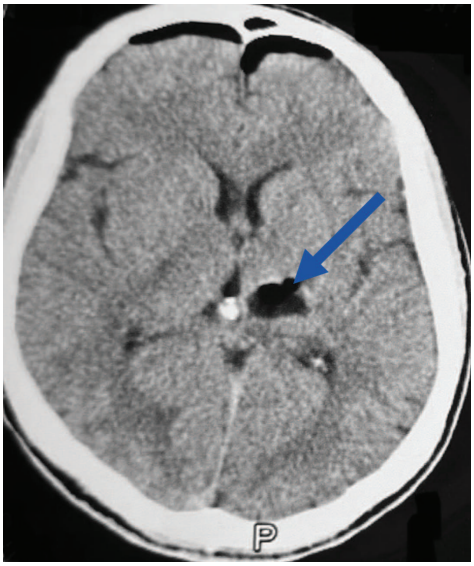


FIG. 3. Resection of the cavernous malformation of the midbrain peduncle via the supracerebellar infratentorial approach in a 38-year-old man (May 28, 2024).
A. General view of the supracerebellar infratentorial approach after opening the dura mater.
B. Incision of the dorsal part of the midbrain, approach to the cavernoma (arrow).
C. Macropreparation of the removed cavernoma 2×3×2.5 cm.

A



B

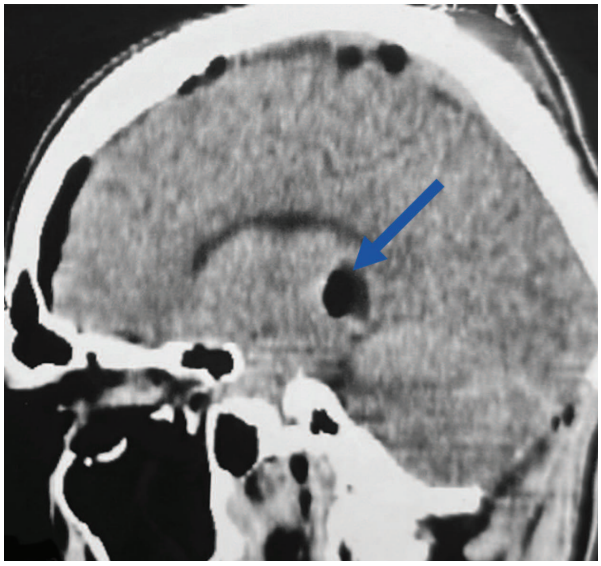
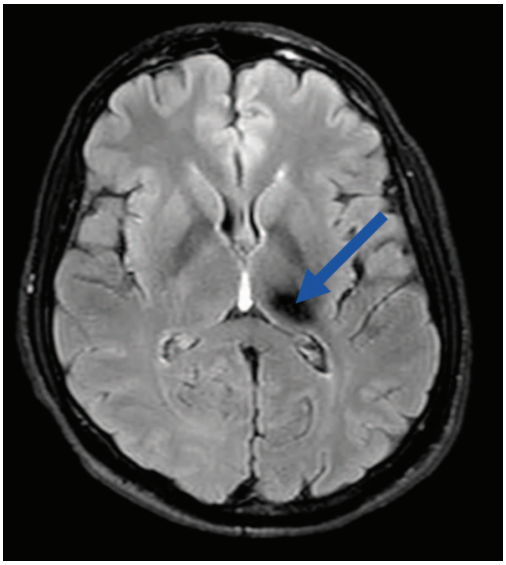


FIG. 4. Computed tomography of a 38-year-old patient on the 4th day after removal of a cavernous malformation in the dorsal part of the left peduncle of the midbrain (June 01, 2024).
A. Axial section: the cavernoma with the hematoma capsule is completely resected (arrow).
B. Sagittal section: the cavernoma with the hematoma capsule is completely resected (arrow).

A



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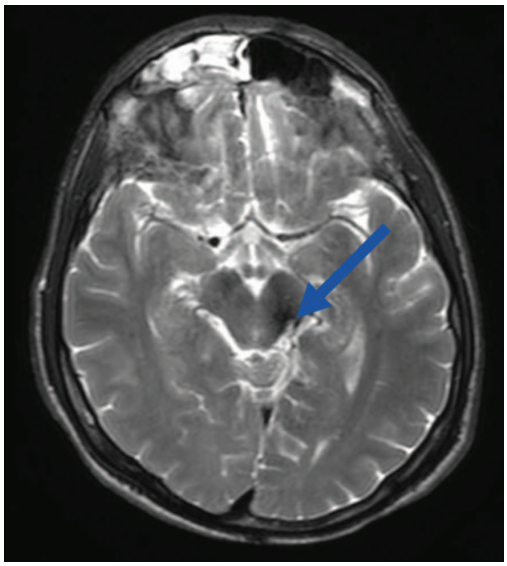

FIG. 5. Magnetic resonance imaging of the brain of a 38-year-old patient 9 months after resection of a cavernous malformation in the dorsal part of the left peduncle of the midbrain (February 18, 2025)
A, B. Axial sections: postoperative gliotic changes (arrows).

The next question concerns the choice of tactics for a safe approach to the midbrain area.

Dorsal lesions are localized in the zones of two thin horizontal lines immediately above and below the quadrigeminal plate. For their surgical treatment, supratentorial suboccipital, occipital transtentorial, supracerebellar infratentorial, posterior subtemporal and tonsillouveal transaqueductal approaches are used [14].

In the presented case, the infratentorial approach to the posterior fossa was used to remove the midbrain CM – this method is most often used by leading neurosurgeons around the world such as M. Lawton and R. Spetzler [3–5]. The two principal craniotomies were used to access the posterior fossa: retrosigmoid (lateral suboccipital) craniotomy and medial suboccipital craniotomy. The retrosigmoid supracrebellar approach was used to reach the lateral midbrain. The medial

suboccipital supracrebellar approach was used to reach the dorsal part of the midbrain and the quadrigeminal plate [15].

The surgical tactics used in the subacute period of hemorrhage from the cavernoma allowed for radical removal of the midbrain CM, ensuring complete neurological recovery of the patient. The patient was able to carry on with his work as usual and there were no signs of a reoccurring hemorrhage (the observation time was 6.5 months).

Knowledge of the brainstem corridors is necessary for planning microsurgical interventions on brainstem formations so as to minimize the risk of damage to nearby structures.

CONCLUSION

The subacute phase of midbrain CM bleeding may be the best time for surgical resection of the cavernoma. The contralateral supracerebellar infratentorial approach is one of the available options for resection of dorsal midbrain CM. It can be considered if the formation is located behind the cerebral peduncle, facing the intrapeduncular fossa and interpeduncular cistern and extends to the dorsal side.

AUTHORS CONTRIBUTIONS

Narzullo O. Rahimov and Khurshed J. Rakhmonov performed surgical treatment and developed the concept of scientific work. Dzhumaboy R. Sanginov, Mahmarajab A. Khasanov developed the methodology for selecting and describing CT and MRI images. Narzullo O. Rahimov collected the material and analyzed the literature data. All authors approved the final version of the publication.

ВКЛАД АВТОРОВ

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INFORMATION ABOUT THE AUTHORS / ИНФОРМАЦИЯ ОБ АВТОРАХ

Narzullo O. Rahimov✉, Cand. of Sci. (Medicine), Associate Professor, Department of Neurosurgery and Combined Trauma, Avicenna Tajik State Medical University; neurosurgeon of the Department of Neurosurgery, SI National Medical Center of Republic of Tajikistan "Shifobakhsh".
ORCID: https://orcid.org/0000-0002-8471-1808

Khurshed J. Rakhmonov, Dr. of Sci. (Medicine), Professor, Department of Neurosurgery and Combined Trauma, Avicenna Tajik State Medical University; Director, SI National Medical Center of Republic of Tajikistan "Shifobakhsh".
ORCID: https://orcid.org/0000-0002-6782-2979

Dzhumaboy R. Sanginov, Dr. of Sci. (Medicine), Professor, Department of Oncology, Avicenna Tajik State Medical University.
ORCID: https://orcid.org/0000-0002-4311-3094

Mukhamadrajab A. Khasanov, resident, Department of Neurosurgery and Combined Trauma, Avicenna Tajik State Medical University.
ORCID: https://orcid.org/0009-0005-3352-0824

Рахимов Нарзулло Одинаевич✉**,** канд. мед. наук, доцент кафедры нейрохирургии и сочетанной травмы ГОУ «ТГМУ им. Абуали ибни Сино»; врач-нейрохирург ГУ «Национальный медицинский центр Республики Таджикистан Шифобахш».
ORCID: https://orcid.org/0000-0002-8471-1808

Рахмонов Хуршед Джамшедович, д-р мед. наук, профессор кафедры нейрохирургии и сочетанной травмы ГОУ «ТГМУ имени Абуали ибни Сино»; директор ГУ «Национальный медицинский центр Республики Таджикистан Шифобахш».
ORCID: https://orcid.org/0000-0002-6782-2979

Сангинов Джумабой Рахматович, д-р мед. наук, профессор кафедры онкологии ГОУ «ТГМУ им. Абуали ибни Сино».
ORCID: https://orcid.org/0000-0002-4311-3094

Хасанов Мухамадраджаб Амридинович, ординатор кафедры нейрохирургии и сочетанной травмы ГОУ «ТГМУ им. Абуали ибни Сино».
ORCID: https://orcid.org/0009-0005-3352-0824

✉ Corresponding author / Автор, ответственный за переписку

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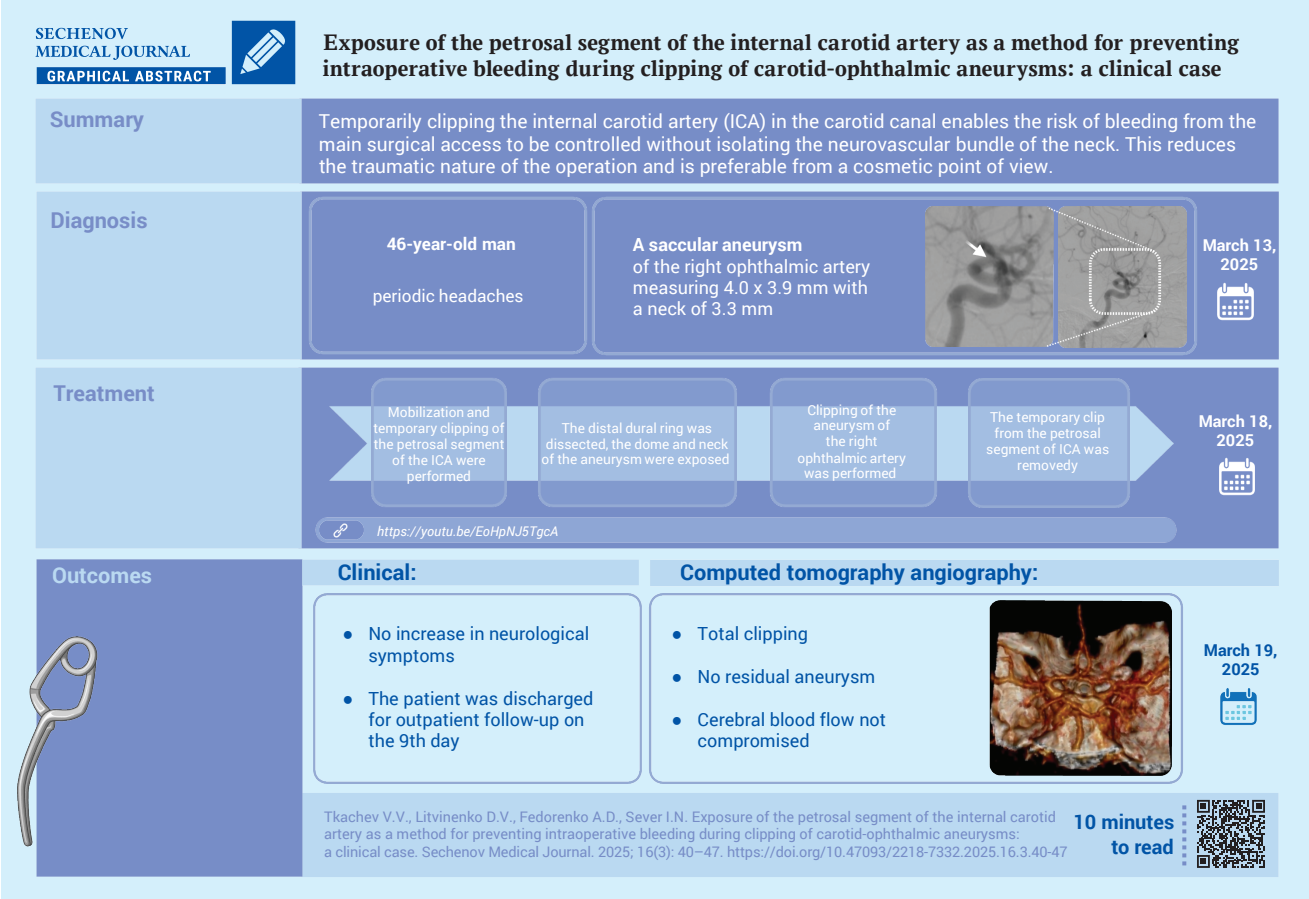
Exposure of the petrosal segment of the internal carotid artery as a method for preventing intraoperative bleeding during clipping of carotid-ophthalmic aneurysms: a clinical case

Vyacheslav V. Tkachev[1,2], Dmitry V. Litvinenko[1,✉], Arkady D. Fedorenko[2], Irina N. Sever[2]
[1] *Scientific Research Institute – Regional Clinical Hospital No. 1 named after professor S.V. Ochapovsky*
167, 1 May str., Krasnodar, 350086, Russia
[2] *Kuban State Medical University*
4, Mitrofan Sedin str., Krasnodar, 350063, Russia



Abstract

Microsurgical treatment of ocular artery aneurysms is classified as high-risk surgery. It is anatomically impossible to prevent and stop bleeding from ophthalmic aneurysms by applying a standard clip proximal to the aneurysm.

Case report. A 46-year-old man was admitted complaining of periodic headaches for 6 months. Outpatient magnetic resonance imaging revealed an aneurysm of the right internal carotid artery (ICA). According to computed tomography and cerebral angiography, an aneurysm of the ocular artery was verified. The patient chose an open surgery from the proposed treatment methods. Clipping of the aneurysm of the ocular artery mouth was performed by pterion access with an extradural extraction of the petrosal segment of the ICA to prevent intraoperative bleeding. The course of the postoperative period was smooth, without neurological symptoms, and the stitches were removed on the 9th day. The patient was discharged under outpatient supervision with a recommendation to control the radicality of clipping after 6 months.

Discussion. Temporary clipping of the ICA in the carotid canal during microsurgical operations for ocular artery aneurysms allows controlling the risk of bleeding from the main surgical access without isolating the neurovascular

bundle of the neck, which reduces the traumatic nature of the operation and is preferable from a cosmetic point of view.

Keywords: carotid-ophthalmic aneurysms; removal of the anterior oblique process; proximal bleeding control; petrosal segment of the internal carotid artery; internal carotid artery mobilization in the carotid canal
MeSH terms:
ANEURYSM – DIAGNOSTIC IMAGING
ANEURYSM – SURGERY
OPHTHALMIC ARTERY – DIAGNOSTIC IMAGING
OPHTHALMIC ARTERY – SURGERY
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CONTACT INFORMATION:
Dmitry V. Litvinenko, Cand. of Sci. (Medicine), neurosurgeon, Department of Neurosergery No. 2, SRI – Regional Clinical Hospital No. 1 named after prof. S.V. Ochapovsky.
Address: 167, May 1 str., Krasnodar, 350086, Russia
E-mail: dlmalit73@yandex.ru

Compliance with ethical standards. Consent statement. The patient consented to the publication of the article "Exposure of the petrous segment of the internal carotid artery as a method for prevention of intraoperative bleeding during clipping of carotid-ophthalmic aneurysms: a clinical case" in the "Sechenov Medical Journal".
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Выделение петрозального сегмента внутренней сонной артерии как метод профилактики интраоперационного кровотечения при клипировании каротидно-офтальмических аневризм: клинический случай

В.В. Ткачев[1,2], Д.В. Литвиненко[1,✉], А.Д. Федоренко[2], И.Н. Север[2]
[1] ГБУЗ «Научно-исследовательский институт – Краевая клиническая больница № 1 имени профессора С.В. Очаповского» Министерства здравоохранения Краснодарского края ул. 1 Мая, д. 167, г. Краснодар, 350086, Россия
[2] ФГБОУ ВО «Кубанский государственный медицинский университет» Министерства здравоохранения Российской Федерации ул. им. Митрофана Седина, д. 4, г. Краснодар, 350063, Россия

Аннотация

Микрохирургическое лечение аневризм глазной артерии относят к хирургии высокого риска. Профилактика и остановка кровотечения из офтальмических аневризм стандартным наложением клипса проксимальнее аневризмы анатомически невозможно.

Описание случая. Пациент 46 лет поступил с жалобами на периодические головные боли в течение шести месяцев. Амбулаторно на магнитно-резонансной томографии выявлена аневризма правой внутренней сонной артерии (ВСА). По данным компьютерно-томографической и церебральной ангиографий верифицирована аневризма глазной артерии. Пациент из предложенных методов лечения выбрал открытую операцию. Проведено клипирование аневризмы устья глазной артерии птериональным доступом с экстрадуральным выделением петрозального сегмента ВСА с целью профилактики интраоперационного кровотечения. Течение послеоперационного периода гладкое, без неврологической симптоматики, швы сняты на 9-е сутки. Пациент выписан под амбулаторное наблюдение с рекомендацией контроля радикальности клипирования через 6 месяцев.

Обсуждение. Временное клипирование ВСА в сонном канале при микрохирургических операциях по поводу аневризм глазной артерии позволяет контролировать кроветечение из основного операционного доступа – без выделения сосудисто-нервного пучка шеи, что снижает травматичность операции и является предпочтительным с косметической точки зрения.

Ключевые слова: каротидно-офтальмические аневризмы; удаление переднего наклоненного отростка; проксимальный контроль кровотечения; петрозальный сегмент внутренней сонной артерии; мобилизация внутренней сонной артерии в сонном канале

Рубрики MeSH:

АНЕВРИЗМА – ДИАГНОСТИЧЕСКОЕ ИЗОБРАЖЕНИЕ
АНЕВРИЗМА – ХИРУРГИЯ
ГЛАЗНАЯ АРТЕРИЯ – ДИАГНОСТИЧЕСКОЕ ИЗОБРАЖЕНИЕ
ГЛАЗНАЯ АРТЕРИЯ – ХИРУРГИЯ
СОННАЯ АРТЕРИЯ ВНУТРЕННЯЯ – ДИАГНОСТИЧЕСКОЕ ИЗОБРАЖЕНИЕ
СОННАЯ АРТЕРИЯ ВНУТРЕННЯЯ – ХИРУРГИЯ
МИКРОХИРУРГИЯ – МЕТОДЫ
ОПЕРАТИВНЫЙ ДОСТУП
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КОНТАКТНАЯ ИНФОРМАЦИЯ:
Литвиненко Дмитрий Викторович, кандидат медицинских наук, врач-нейрохирург нейрохирургического отделения № 2 ГБУЗ «НИИ – Краевая клиническая больница № 1 им. профессора С.В. Очаповского» Минздрава Краснодарского края
Адрес: ул. 1 Мая, д. 167, г. Краснодар, 350086, Россия
E-mail: dlmalit73@yandex.ru

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Финансирование. Исследование не имело спонсорской поддержки (собственные ресурсы).

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Abbreviations:
ICA – internal carotid artery

HIGHLIGHTS

Despite the development of endovascular methods, proximal bleeding control for carotid-ophthalmic aneurysms is carried out through open intervention.

Temporary clipping of the internal carotid artery in the carotid canal through the Kawase triangle effectively prevents intraoperative bleeding without accessing the neck vessels.

The proposed modified technique for proximal control in the carotid canal is anatomically gentle, since it preserves the auditory tube, greater petrosal and trigeminal nerves, does not require mobilization of the temporal lobe pole and reduces the risk of vascular wall injury.

Open exclusion of carotid-ophthalmic aneurysms is a non-trivial task due to the peculiarities of their anatomy [1], inaccessibility, difficulty in stopping possible bleeding from the aneurysm, as well as the risks of deterioration of visual functions [2]. Currently, the choice of treatment for ophthalmic aneurysms is intravascular interventions, but a significant proportion of patients continue to undergo open surgeries for various reasons [3].

The issue of prevention and effective control of bleeding remains a cornerstone of microsurgery for ophthalmic aneurysms. Proximal bleeding control is traditionally achieved by dissecting the cervical segment of the internal carotid artery (ICA), which de facto means performing an additional operation with potential complications and cosmetic defects [4]. The use of temporary clipping of the ICA in the carotid canal allows for the effective cessation of antegrade blood flow in the proximal segments of the ICA without dissection of the cervical neurovascular bundle, thereby reducing the trauma of the operation and the risks of perioperative complications and improving cosmetic results [5–7].

The aim of this case report is to demonstrate the experience of temporary clipping of the ICA in the carotid canal using an open approach during microsurgical exclusion of an aneurysm of the right ophthalmic artery.

CASE REPORT

A 46-year-old patient was admitted to the clinic of the Scientific Research Institute – Regional Clinical Hospital No. 1 named after Prof. S. V. Ochapovsky on March 13, 2025. The patient complained of periodic headaches that had been bothering him for the past six months. An outpatient magnetic resonance imaging scan of the brain revealed an aneurysm of the right ICA. The patient was hospitalized for digital subtraction cerebral angiography and surgical treatment. On examination: the neurological status without focal neurological symptoms, the somatic status without abnormalities. Computed tomography angiography and cerebral angiography verified a saccular aneurysm of the right ophthalmic artery measuring 4.0×3.9 mm with a neck of 3.3 mm (Fig. 1A–D).

After consultation with endovascular surgeons, the patient was offered a choice: endovascular treatment using an intracranial stent or open aneurysm exclusion. The potential risks of open and endovascular treatment were explained. The patient preferred open surgery and signed the relevant consent form.

Surgical technique

The operation was performed on March 18, 2025. A limited incision of the dura mater was made using the standard pterional approach. The cistern of the lateral cerebral fossa (Sylvian cistern) was opened to relax the brain. An extradural subfrontal approach was used to resect the lesser wing of the sphenoid bone and remove the anterior clinoid process. Hemostasis was achieved. After the final opening of the dura mater and dissection of the basal cisterns, the optic nerve, ICA, and aneurysm dome were identified.

An extradural subtemporal approach to the anterior surface of the temporal bone pyramid was performed to ensure proximal control of possible bleeding. The foramen spinosum and foramen ovale were identified. Partial peeling of the outer wall of the cavernous sinus was performed, exposing the mandibular nerve. The greater petrosal nerve was identified.

After skeletonization of the apex of the petrous bone and trepanation of the upper wall of the carotid canal (Fig. 2A), mobilization and temporary clipping of the petrosal segment of the ICA were performed (Fig. 2B). Then the distal dural ring was dissected, the dome and neck of the aneurysm were exposed (Fig. 2C). Clipping of the aneurysm of the right ophthalmic artery was performed (Fig. 2D). After checking the patency of the ophthalmic artery, coagulation of the aneurysm dome was performed. The temporary clip from the ICA was removed, hemostasis was achieved in the area of the petrous segment of the ICA, and the surgical wound was sutured. A video of the operation is available at the link: https://youtu.be/EoHpNJ5TgcA.

The postoperative period was uneventful, with no increase in neurological symptoms. Follow-up computed tomography and computed tomography angiography scans performed one day after surgery (March 19, 2025) revealed no residual aneurysm (Fig. 3A–C). The wound healed by primary tension, the sutures were removed on the 9th day, and the patient was discharged for outpatient follow-up with a recommendation to check the radicality of clipping in 6 months.

DISCUSSION

Performing open surgeries on cerebral aneurysms is associated with an increased risk of intraoperative bleeding during dissection of the aneurysm dome and neck [8].

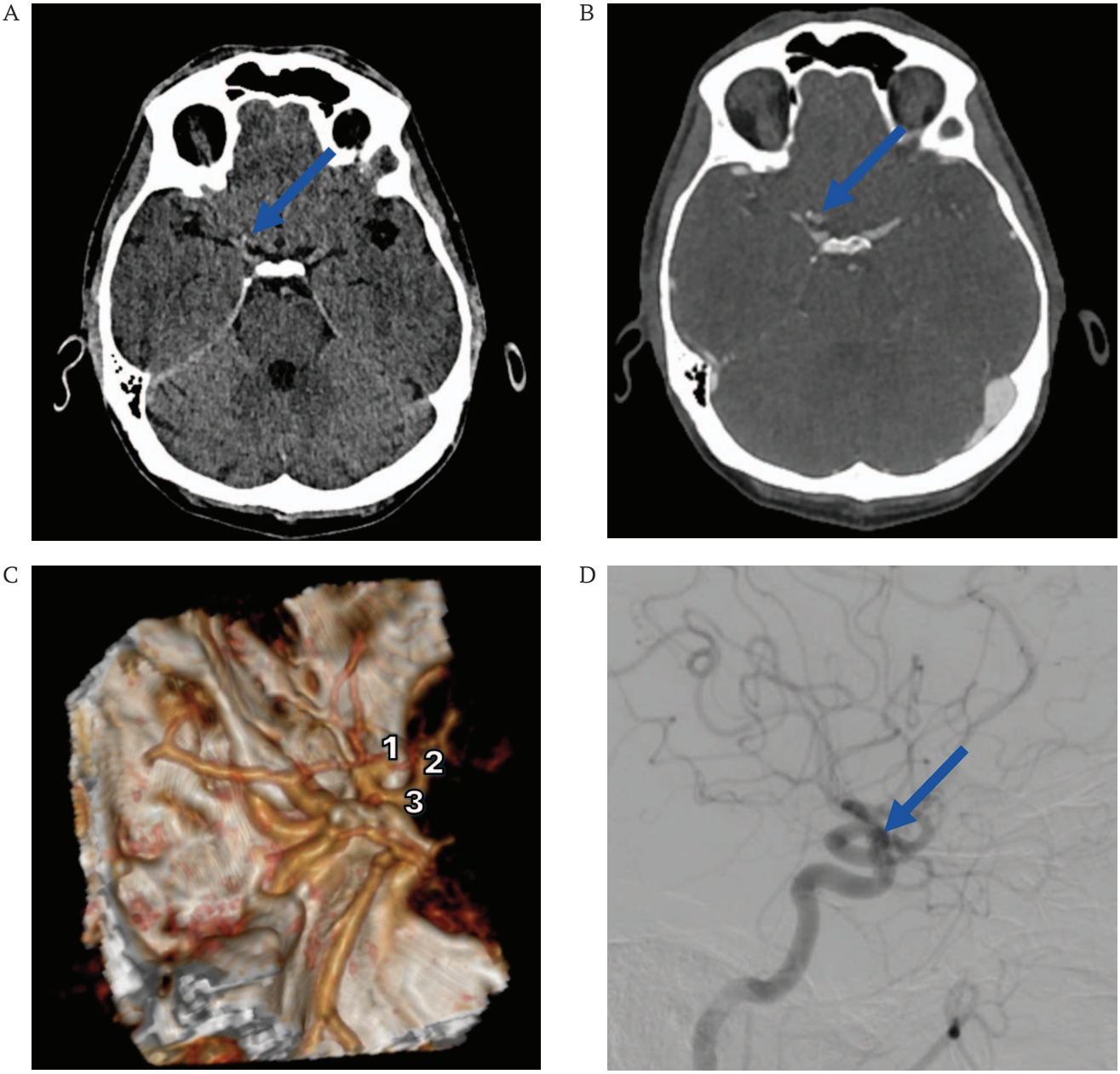

FIG. 1. Computed tomography (A), computed tomography angiography (B, C), and cerebral angiography (D) of a 46-year-old patient with an aneurysm of the ophthalmic artery orifice before surgery.
A, B. Axial section: aneurysm dome (arrow), no signs of hemorrhage.
C. 3D reconstruction: 1 – aneurysm dome, 2 – M2 segment of the middle cerebral artery, 3 – C7 segment of the internal carotid artery.
D. Lateral projection: aneurysm dome (arrow).

Patients with ophthalmic artery aneurysms, which are anatomically complex and difficult to access for surgery, are operated on mostly using intravascular methods. These include occlusion using microcoils: balloon and stent assistance, as well as the installation of flow-diverting devices [9–11].

In open surgery, prevention and control of bleeding from intradural and transit aneurysms of the ophthalmic segment of the ICA are particularly important, since routine application of temporary clips proximal to the aneurysm is impossible due to anatomical conditions. To date, the main method for controlling bleeding from ophthalmic aneurysms remains the exposure of the bifurcation of the common carotid artery into the internal and external branches in the neck. This method of proximal control involves the use of a second surgical approach with possible complications: paresis of the vocal cords and tongue; hematoma in the surgical area, causing compression of the trachea and severe breathing difficulties, in some cases requiring intubation or

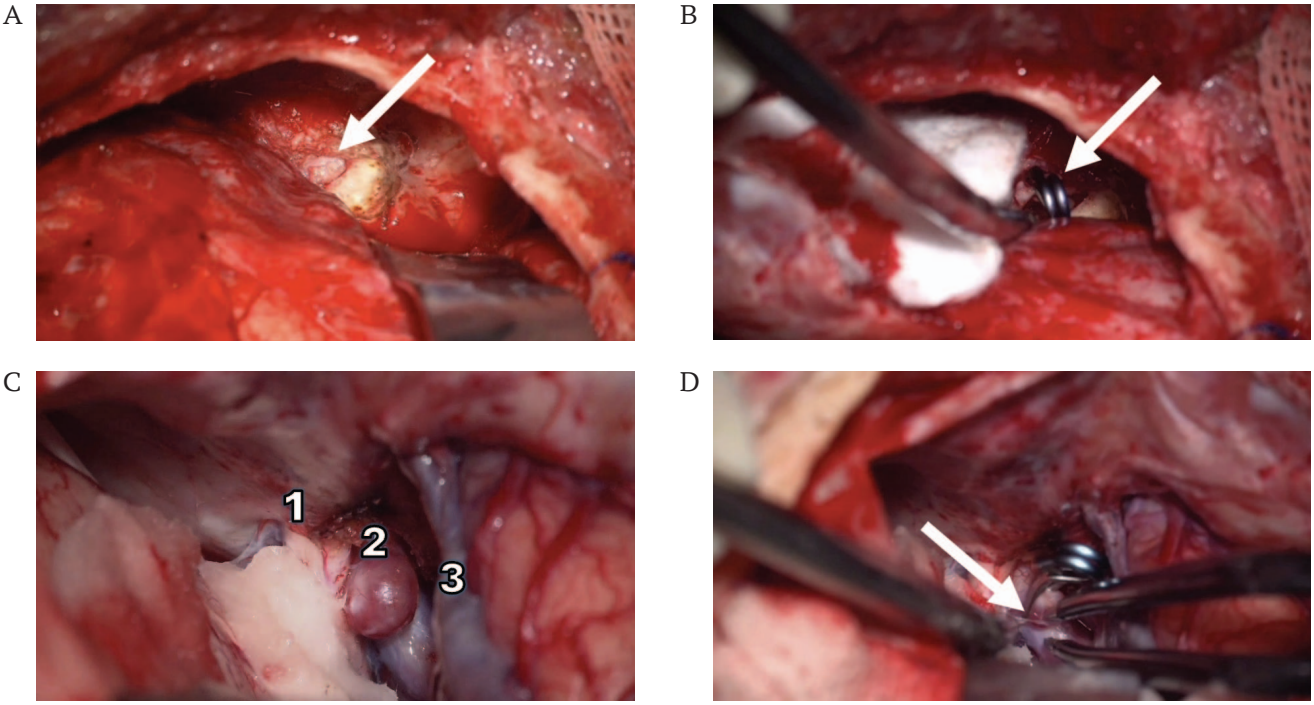

FIG. 2. Clipping of the aneurysm of the right ophthalmic artery orifice in a 46-year-old patient.
A. Removal of the superior wall of the carotid canal, exposure of the petrous segment of the internal carotid artery (arrow).
B. Temporary clipping of the C2 internal carotid artery (arrow).
C. Dissection of the aneurysm of the ophthalmic artery orifice: 1 – optic nerve, 2 – aneurysm dome, 3 – internal carotid artery.
D. Clipping of the ophthalmic artery aneurysm (arrow).

tracheostomy; dissection of the exposed arteries. Access to the neck vessels may be difficult or impossible in the presence of cicatricial adhesive process after previous surgery or radiation therapy [4].

Occlusion of the ICA in the neck often does not lead to complete cessation of antegrade blood flow through the ophthalmic segment, which is associated with the presence of distal anastomoses between the ICA and branches of other brachiocephalic arteries [12].

Methods for mobilizing the ICA proximal to its cerebral portion, in the ICA carotid canal, were proposed quite some time ago [6, 7], but they did not become widely used due to the complexity of their technical implementation and the presence of a number of shortcomings. The intradural access to the petrosal part of the ICA proposed by T.M. Wascher et al. [6], involved complete mobilization of the temporal lobe pole, which significantly increased the risk of developing venous cerebral infarction in the surgical area, and the use of a balloon catheter for occlusion of the ICA carried the risks of incomplete occlusion or excessive compression, leading to damage to the arterial wall.

In the technique described by L.N. Sekhar et al. [7], orbitomaxillofacial craniotomy was proposed for the isolation of the petrosal segment of the ICA, which made the operation more traumatic and worsened cosmetic results. In addition, in all cases, when drilling the carotid canal in the posterolateral triangle (Glasscock triangle) required opening the bony part of the auditory tube, which increased the risk of developing inflammation of the middle ear inflammation and hearing loss. Both techniques involved transection of the greater petrosal nerve, creating a potential risk of complications due to denervation of the lacrimal gland on the access side.

In the described case, a modified method of proximal bleeding control was used (video) [5]. To perform this procedure, after standard pterional craniotomy, the upper wall of the carotid canal in the posteromedial triangle (Kawase triangle) is resected using an extradural approach. The roots of the trigeminal and greater petrosal nerves are preserved; the Eustachian tube, cochlea, and internal auditory canal remain intact. The ICA is mobilized in a sheath of periosteum lining the walls of the carotid canal, which minimizes its trauma, and occlusion of the ICA with clips with a specified degree of compression of their branches reliably stops blood flow without damaging the vascular wall.

CONCLUSION

The use of modern methods of proximal bleeding control during open surgery in patients with aneurysms of the ophthalmic segment of the ICA, including temporary clipping of the petrosal segment of the ICA, allows for the optimization of surgical technique. This results in increasing the safety of the intervention due to

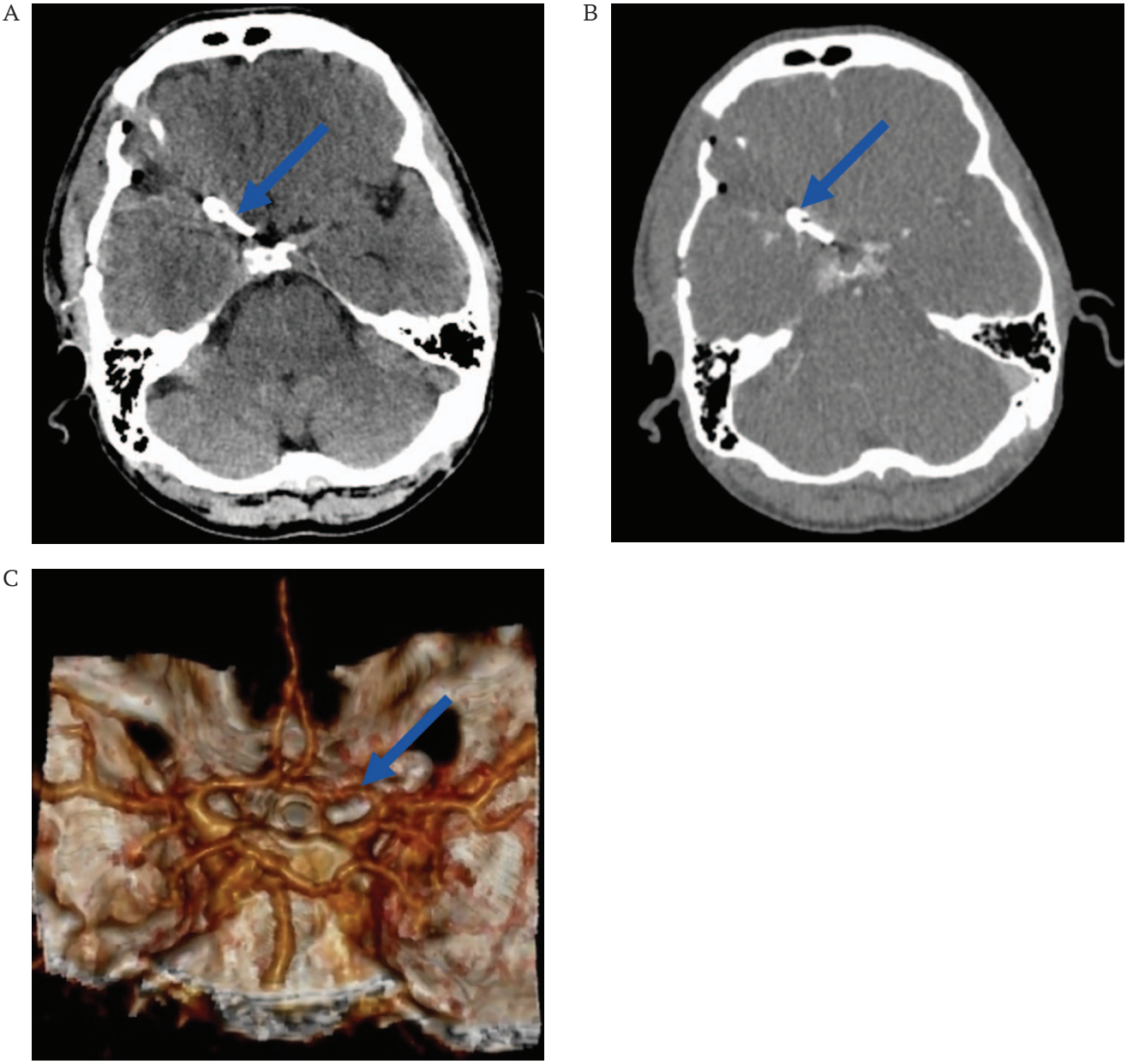

FIG. 3. Computed tomography (A), computed tomography angiography (B, C) of a 46-year-old patient with an aneurysm of the ophthalmic artery ostium 24 hours after surgery. Total clipping, cerebral blood flow not compromised.
A, B. Axial section: clip on the aneurysm (arrow).
C. 3D reconstruction: clip on the aneurysm (arrow).

the reliable prevention of bleeding, as well as minimizing the amount of tissue trauma, and improving cosmetic and functional outcomes. All of these factors are important for the patient's quality of life.

AUTHOR CONTRIBUTIONS

Vyacheslav V. Tkachev performed the surgery, made the main contribution to the concept and design of the article, and supervised the writing and editing process. Dmitry V. Litvinenko, Arkady D. Fedorenko participated in the development of the concept and design of the article, writing and editing the text, as well as preparing illustrations and video. Irina N. Sever participated in the analysis of literature data, processing of illustrations and video, editing the text. All authors approved the final version of the article.

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В.В. Ткачев выполнил хирургическую операцию, внес основной вклад в концепцию и дизайн статьи, а также руководил процессом написания и редактирования. Д.В. Литвиненко, А.Д. Федоренко участвовали в разработке концепции и дизайна статьи, написании и редактировании текста, а также подготовке иллюстраций и видео. И.Н. Север участвовала в анализе данных литературы, обработке иллюстраций и видео, редактировании текста. Все авторы одобрили окончательный вариант статьи и готовы взять на себя ответственность за все аспекты представленной публикации.

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INFORMATION ABOUT THE AUTHORS / ИНФОРМАЦИЯ ОБ АВТОРАХ

Vyacheslav V. Tkachev, Dr. of Sci. (Medicine), Professor, Department of Neurology and Neurosurgery, Associate Professor, Department of Surgery No. 1, Kuban State Medical University; Head of the Department of Neurosurgery No. 2, SRI – Regional Clinical Hospital No. 1 named after prof. S.V. Ochapovsky.
ORCID: https://orcid.org/0000-0002-5600-329X

Dmitry V. Litvinenko✉, Cand. of Sci. (Medicine), neurosurgeon, Department of Neurosergery No. 2, SRI – Regional Clinical Hospital No. 1 named after prof. S.V. Ochapovsky.
ORCID: https://orcid.org/0000-0002-4831-1874

Arkady D. Fedorenko, resident, Department of Neurology and Neurosurgery, Kuban State Medical University.
ORCID: https://orcid.org/0009-0004-1461-553X

Irina N. Sever, postgraduate student, Department of Neurology and Neurosurgery, Kuban State Medical University.
ORCID: https://orcid.org/0009-0008-4737-3994

Ткачев Вячеслав Валерьевич, д-р мед. наук, профессор кафедры неврологии и нейрохирургии, доцент кафедры хирургии № 1 ФГБОУ ВО КубГМУ Минздрава России; заведующий нейрохирургическим отделением № 2 ГБУЗ «НИИ – Краевая клиническая больница № 1 им. профессора С.В. Очаповского» Минздрава Краснодарского края.
ORCID: https://orcid.org/0000-0002-5600-329X

Литвиненко Дмитрий Викторович✉, канд. мед. наук, врач-нейрохирург нейрохирургического отделения № 2 ГБУЗ «НИИ – Краевая клиническая больница № 1 им. профессора С.В. Очаповского» Минздрава Краснодарского края.
ORCID: https://orcid.org/0000-0002-4831-1874

Федоренко Аркадий Дмитриевич, ординатор кафедры неврологии и нейрохирургии ФГБОУ ВО КубГМУ Минздрава России.
ORCID: https://orcid.org/0009-0004-1461-553X

Север Ирина Николаевна, аспирантка кафедры неврологии и нейрохирургии ФГБОУ ВО КубГМУ Минздрава России.
ORCID: https://orcid.org/0009-0008-4737-3994

✉ Corresponding author / Автор, ответственный за переписку

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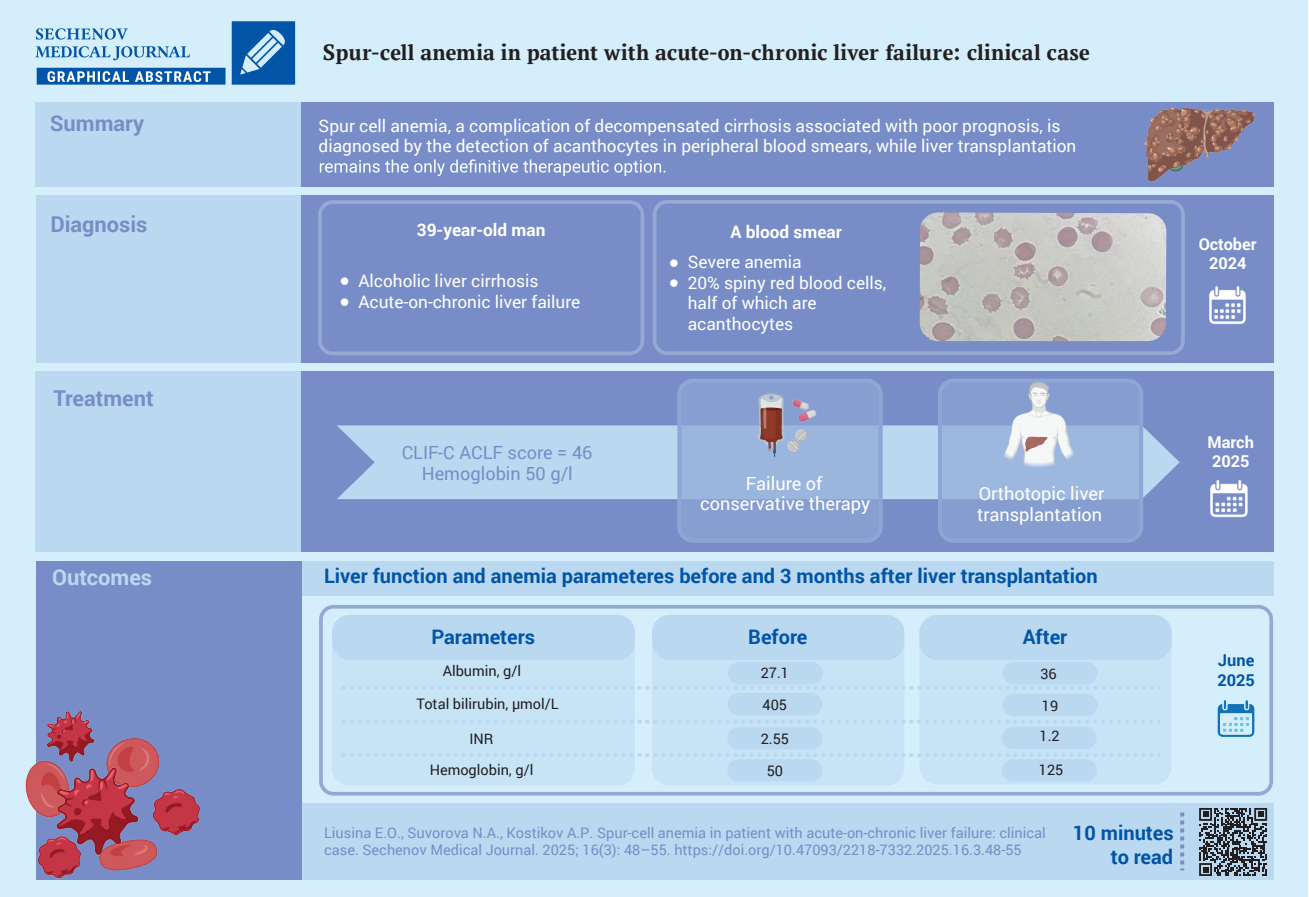
Spur-cell anemia in patient with acute-on-chronic liver failure: clinical case

Ekaterina O. Liusina[1,2,✉], Natalia A. Suvorova[3,4,5], Andrey P. Kostikov[6]
[1]National Medical Research Center for Therapy and Preventive Medicine
10/3, Petroverigsky Ln., Moscow, 101990, Russia
[2]LLC "Chaika White Gardens"
9, Lesnaya str., Moscow, 125196, Russia
[3]N.I. Pirogov Russian National Research Medical University
1/6, Ostrovityanova str., Moscow, 117513, Russia
[4]City Clinical Hospital No.15 named after O.M. Filatov
23, Veshnyakovskaya str., Moscow, 111539, Russia
[5] LLC "DOCMED"
35, Trubnaya str., Moscow, 127051, Russia
[6] LLC "Children's Clinic"
21, Palekhskaya str., Moscow, 129337, Russia



Abstract

One of the rare forms of anemia in patients with liver cirrhosis (LC) is acanthocytosis (spur cell anemia) – a non-immune hemolytic anemia caused by alterations in the lipid composition of the red blood cells membrane because of severe liver failure.

Case report. A 37-year-old patient with decompensated alcoholic LC (Child-Pugh class C, the MELD-Na (Model for End-Stage Liver Disease – Na) score was 34 points) presented with severe weakness and dyspnea. Acute-on-chronic liver failure was diagnosed: CLIF-C ACLF (Chronic Liver Failure Consortium Acute-on-Chronic Liver Failure Score) score was 46. Severe macrocytic anemia with reticulocytosis was detected: hemoglobin – 50 g/L, red blood cells – 1.26×10^{12}/L, reticulocytes – 77.9 ‰. Other causes of anemia, such as blood loss, iron deficiency, vitamin B_{12} and folate deficiencies were excluded. The Coombs test was negative, and bone marrow examination ruled out myelodysplasia. Blood smear analysis revealed that 20% of red blood cells had the shape of spur cells, with approximately half of them being acanthocytes. Orthotopic liver transplantation was performed. Follow-up examination after three months showed normalization of liver function tests and absence of anemia and acanthocytosis.
Discussion. This case report highlights the need for blood smear examination to detect acanthocytes – a rare but prognostically unfavorable cause of anemia in patients with LC. Liver transplantation remains the only effective treatment option.

Keywords: spur-cell anemia; hemolysis; cirrhosis; alcohol; acanthocytes; MELD-Na; CLIF-C ACLF; liver transplantation
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CONTACT INFORMATION:
Ekaterina O. Liusina, Cand. of Sci. (Medicine), Research Associate, Laboratory of Experimental and Preventive Gastroenterology, National Medical Research Center for Therapy and Preventive Medicine; gastroenterologist, LLC "Chaika White Gardens".
Address: 9, Lesnaya str., Moscow, 125196, Russia
E-mail: eka-lusina@yandex.ru

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Акантоцитоз – редкая причина анемии у пациента с острым повреждением печени на фоне хронического: клинический случай

Е.О. Люсина[1,2,✉], Н.А. Суворова[3,4,5], А.П. Костиков[6]

[1]ФГБУ «Национальный медицинский исследовательский центр терапии и профилактической медицины» Министерства здравоохранения Российской Федерации
пер. Петроверигский, д. 10, стр. 3, г. Москва, 101990, Россия
[2]ООО «Чайка Белые Сады»
ул. Лесная, д. 9, г. Москва, 125196, Россия
[3]ФГАОУ ВО «Российский национальный исследовательский медицинский университет имени Н.И. Пирогова» Министерства здравоохранения Российской Федерации
ул. Островитянова, д. 1, стр. 6, г. Москва, 117513, Россия
[4]ГБУЗ «Городская клиническая больница № 15 имени О.М. Филатова Департамента здравоохранения города Москвы»
ул. Вешняковская, д. 23, г. Москва, 111539, Россия
[5] ООО «ДОКМЕД»
ул. Трубная, д. 35, г. Москва, 127051, Россия
[6]ООО «Детская клиника»
ул. Палехская, д. 21, г. Москва, 129337, Россия

Аннотация

Одной из редких форм анемии у пациентов с циррозом печени (ЦП) является акантоцитоз (шпороклеточная анемия) – неиммунная гемолитическая анемия, обусловленная изменением липидного состава мембраны эритроцитов в результате тяжелой печеночной недостаточности.

Описание случая. У пациента 37 лет с декомпенсированным алкогольным ЦП (класс С по шкале Child – Pugh, индекс MELD-Na (Model for End-Stage Liver Disease – Na, модель для оценки терминальной стадии заболевания печени с учетом натрия) составил 34 балла) появилась выраженная слабость и одышка. Диагностировано острое повреждение печени на фоне хронического: показатель по шкале CLIF-C ACLF (Chronic Liver Failure Consortium Acute-on-Chronic Liver Failure Score, шкала оценки острого повреждения печени на фоне хронического Консорциума по изучению хронической печеночной недостаточности) составила 46 баллов. Выявлена тяжелая макроцитарная анемия с ретикулоцитозом: гемоглобин – 50 г/л, эритроциты – $1{,}26\times10^{12}$/л, ретикулоциты – 77,9 ‰. Исключена кровопотеря, дефицит железа, витамина B_{12} и фолатов, проба Кумбса отрицательная, исследование костного мозга исключило миелодисплазию. В мазке крови 20% эритроцитов имели форму шпоровидных клеток, из них около половины – акантоциты. Выполнена ортотопическая трансплантация печени. Контрольное обследование через три месяца показало нормализацию печеночных функциональных тестов и отсутствие анемии и акантоцитоза.

Обсуждение. Представленный случай демонстрирует необходимость изучения мазка крови для выявления акантоцитов как редкой, но прогностически неблагоприятной причины анемии у пациентов с ЦП. Единственным эффективным методом лечения является трансплантация печени.

Ключевые слова: шпороклеточная анемия; гемолиз; цирроз; алкоголь; акантоциты; MELD-Na; CLIF-C ACLF; трансплантация печени

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КОНТАКТНАЯ ИНФОРМАЦИЯ:
Люсина Екатерина Олеговна, канд. мед. наук, научный сотрудник лаборатории экспериментальной и профилактической гастроэнтерологии ФГБУ «НМИЦ терапии и профилактической медицины» Минздрава России; врач-гастроэнтеролог ООО «Чайка Белые Сады».
Адрес: ул. Лесная, д. 9, г. Москва, 125196, Россия
E-mail: eka-lusina@yandex.ru

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Abbreviations:
ACLF – acute-on-chronic liver failure
LC – liver cirrhosis
SCA – spur cell anemia

HIGHLIGHTS

Acanthocytosis (spur cell anemia) in a patient with liver cirrhosis is a rarely diagnosed but highly unfavorable prognostic form of anemia, particularly in the setting of acute-on-chronic liver failure.

The diagnosis of acanthocytosis is based on microscopic examination of a peripheral blood smear.

Liver transplantation is the only effective treatment option for spur cell anemia in patients with liver cirrhosis.

Anemia is a common complication of liver cirrhosis (LC), occurring in 66–75% of patients, and is associated with a higher rate of cirrhosis decompensation, hospital admissions, development of acute-on-chronic liver failure (ACLF), reduced survival, and increased mortality [1, 2]. The most common etiological factors of anemia in LC patients are iron, folic acid, and vitamin B_{12} deficiencies, as well as chronic inflammation.

One of the least studied and rarely diagnosed forms of anemia in patients with LC is spur cell anemia (SCA) — a type of non-immune hemolytic anemia that develops because of abnormalities in the lipid composition of red blood cells membranes. In particular, there is an increase in the cholesterol-to-phospholipid and protein ratio, which in turn increases membrane rigidity, reduces its fluidity, and leads to mechanical damage of the cells. In addition, fatty acid metabolism is disrupted: their incorporation into phosphatidylethanolamine decreases, while incorporation into acylcarnitine increases. Such disturbances are characteristic of all forms of SCA, as they impair the restoration of membrane lipids and lead to the formation of characteristic protrusions (spurs) on the red blood cells surface, which can be observed under blood smear microscopy [3].

Spur-shaped red blood cells (acanthocytes) undergo hemolysis and are eliminated by the mononuclear phagocyte system. The standard diagnostic criterion for SCA is the detection of more than 5% acanthocytes in a blood smear with a hemoglobin level below 100 g/L and the exclusion of other causes of anemia [4].

The development of SCA in patients with LC is associated with an unfavorable prognosis, frequent episodes of decompensation, and higher mortality rates [5–7].

Currently there is no effective treatment for SCA; various pharmacological agents with different mechanisms of action and plasmapheresis have been described, although it is underlined that only liver transplantation leads to resolution of the anemia [8].

The aim of this case report is to demonstrate the development of secondary acanthocytosis in a patient with severe hepatic dysfunction and to increase clinicians' awareness of this rare etiology of anemia.

CASE REPORT

A 37-year-old male patient, technical specialist with a history of alcohol abuse over the past 3–5 years first noted scleral icterus in November 2023. Laboratory tests revealed elevated levels of bilirubin, alanine aminotransferase, aspartate aminotransferase, and gamma-glutamyl transpeptidase. Viral and autoimmune etiologies of liver disease, Wilson's disease, and hereditary haemochromatosis were excluded. The patient had no metabolic risk factors, and ultrasonography of the liver showed no signs of steatosis, which allowed the exclusion of metabolic dysfunction-associated steatotic liver disease. Upon alcohol abstinence, jaundice regressed.

In April 2024, the patient developed recurrent jaundice. Laboratory tests revealed hyperbilirubinemia, elevated alanine aminotransferase, aspartate aminotransferase, and gamma-glutamyl transpeptidase, hypoalbuminemia, moderate thrombocytopenia, and a slight decrease in hemoglobin to 121 g/L (Table). Imaging investigations showed signs of portal hypertension (grade 2 esophageal varices, minimal ascites, splenomegaly). A diagnosis of severe alcoholic hepatitis (Maddrey's discriminant function was 41) and LC was established. The patient responded to treatment with prednisolone 40 mg/day: on the day 7th, the Lille score was 0.06, which after prednisolone was gradually tapered and discontinued. During therapy, the severity of jaundice decreased, although complete regression was not achieved.

In August 2024, the patient's condition deteriorated, with the onset of weakness, dyspnea, ascites, and oedema. Laboratory tests revealed hyperbilirubinemia, marked hypoalbuminemia, severe anemia (hemoglobin – 79 g/L), elevated C-reactive protein, and deficiencies of vitamin B_{12} (159 pg/mL) and folates (1.9 ng/mL) (Table). Iron metabolism indices were within the reference ranges. The severity of LC was classified as Child–Pugh C, MELD-Na (Model for End-Stage Liver Disease – Na) was 25 points. The anemia was initially attributed to vitamin B_{12} and folate deficiency. Treatment included albumin infusions, a single erythrocyte transfusion, spironolactone, furosemide, rifaximin, vitamin B_{12}, folic acid, and thiamine. Improvement was observed, with reduction in oedema and ascites, some alleviation of weakness and dyspnea, and a transient increase in hemoglobin to 85 g/L.

During the following month, progressive weakness, dyspnea, and oedema recurred. The patient was readmitted in October 2024. On examination: body temperature 36.5 °C, oxygen saturation 98%, clear consciousness

***Table*. Dynamics of laboratory parameters in a patient with liver cirrhosis**

Parameter	Ref. range	Nov. 2023	Apr. 2024	Aug. 2024	Oct. 2024	Jul. 2025
Complete Blood Count						
hemoglobin, g/l	130–170	132	121	79	50	125
red blood cells, $\times10^{12}$/l	4.3–5.7	4.2	3.5	2.3	1.3	4.0
reticulocytes, ‰					77.9	5.1
white blood cells, $\times10^{9}$/l	4.5–11.0	6.5	6.9	8.4	15.6	4.1
Neutrophils, $\times10^{9}$/l	1.78–5.38			5.2	11.1	2.0
Plateles, $\times10^{9}$/l	150–400	137	80	47	86	124
Biochemistry						
albumin, g/l	35–52		31.2	27.6	27.1	36.0
ALT, U/l	<35	80	58	27	13	12
AST, U/l	<35	230	72	82	52	17
LDH, U/l					671	182
GGTP, U/l	<49	938	526	621	749	32
total bilirubin, μmol/l	3.4–20.5	42	214	273	405	
direct bilirubin, μmol/l	<8.6	34	176	207	172	
creatinine, μmol/l	49–90	70	95	110	152	127
cholesterol, mmol/l	<5.0	6.7		2.5	1.9	3.2
C-reactive protein, mg/L	<5.0			36	20	3
Coagulation panel						
INR	0.8–1.2	1.13	1.75	1.65	2.55	1.20
prothrombin time, sec	9.4–12.5		18.7		23.4	
fibrinogen, g/l	2.0–4.0	3.1	2.6	1.5	1.8	2.4

Note: ALT – alanine aminotransferase; AST – aspartate aminotransferase; GGTP – gamma-glutamyltranspeptidase; INR – international normalized ratio; LDH – lactate dehydrogenase.

(Glasgow Coma Scale score was 15), no signs of overt hepatic encephalopathy. The skin, sclerae, and visible mucosae were icteric, lower extremities oedema were present. Heart rate was 83 bpm, blood pressure – 115/75 mmHg. The abdomen was enlarged due to non-tensed ascites, non-tender on palpation, hepatosplenomegaly was noted.

Abdominal ultrasound showed grade 2 ascites, hepatosplenomegaly, and dilation of the portal and splenic veins. Upper endoscopy showed grade 2 oesophageal varices.

Laboratory tests demonstrated persistent marked hyperbilirubinemia involving both fractions, elevated gamma-glutamyltranspeptidase, impaired hepatic protein-synthetic function (hypoproteinemia, hypoalbuminemia, hypocholesterolemia, hypocoagulation), elevated C-reactive protein, and increased creatinine up to 152 µmol/L.

A complete blood count revealed severe macrocytic anemia with reticulocytosis: hemoglobin – 50 g/L, red blood cells – 1.26×10^{12}/L, reticulocytes – 77.9 ‰, MCV (mean corpuscular volume) – 126 fL; moderate thrombocytopenia (platelets – 86×10^{9}/L), and leukocytosis (white blood cells – 15.6×10^{9}/L) with a left shift (Table).

Urinalysis showed increased urobilinogen and direct bilirubin, but no free hemoglobin, proteinuria or urinary sediment abnormalities.

A diagnostic workup for the causes of anemia was conducted. Occult blood was not detected in stool samples (tested twice). Iron metabolism parameters — serum iron (26 µmol/L), transferrin saturation (47%), and latent iron-binding capacity (24.9 µmol/L) — were within reference limits, excluding iron deficiency. Serum vitamin B_{12} (201.4 pg/mL) and folic acid (9.2 ng/mL) concentrations were within normal ranges. Lactate dehydrogenase levels were elevated, and the direct Coombs test was negative.

A peripheral blood smear demonstrated anisocytosis (macrocytosis), poikilocytosis, spherocytes, target cells, and 20% of red blood cells with spur-like morphology, approximately half of which were acanthocytes. Howell–Jolly bodies were observed in some red blood cells (Figure). The patient was examined by a hematologist, and sternal puncture revealed erythroid hyperplasia. To exclude hypothyroidism as a potential cause of secondary acanthocytosis, thyroid-stimulating hormone was measured (2.5 mIU/L), which was within the reference range.

Thus, in a patient with toxic etiology liver cirrhosis (Child–Pugh class C, MELD-Na was 34), ACLF was diagnosed: CLIF-C ACLF (Chronic Liver Failure Consortium Acute-on-Chronic Liver Failure score)[1] score was 46. The severity of ACLF was grade 2 with the development of hepatic failure and acute kidney injury of prerenal origin stage 1 according to KDIGO (Kidney Disease: Improving Global Outcomes). Based on hematological evaluation, secondary acanthocytosis was diagnosed in the patient with severe hepatic failure.

Treatment of LC and its complications was conducted in accordance with the clinical guidelines of the Ministry of Health of the Russian Federation[2]. To correct anemia, three packed red blood cell transfusions were performed, achieving a maximum hemoglobin level of 71 g/L.

The patient met the criteria for severe decompensated LC with signs of poor prognosis, which justified consultation with a transplant specialist and placement on the liver transplantation waiting list. In spring 2025, orthotopic liver transplantation was performed. The surgical procedure was completed without complications, appropriate immunosuppressive therapy was administered, and three months post-transplantation, anemia resolved: hemoglobin was 125 g/L, red blood cells – 4.0×10^{12}/L, and no acanthocytes were detected (Table).

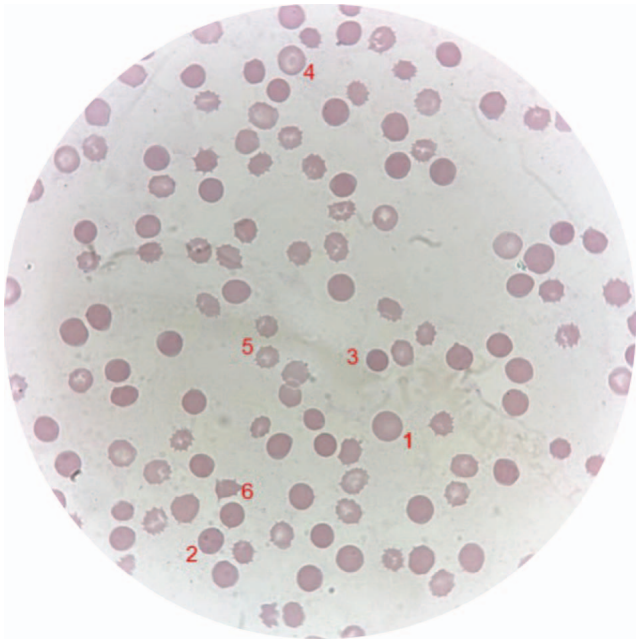

FIG. Peripheral blood smear, Romanowsky–Giemsa stain, magnification ×1000.

Note: 1 – normal red blood cell; 2 – pathological red blood cell inclusions (Howell–Jolly bodies); 3 – spherocyte; 4 – target cell; 5 – spur cell: echinocyte (uniform, evenly distributed spicules); 6 – spur cell: acanthocyte (irregular, unevenly distributed spicules).

[1] Chronic Liver Failure Consortium Acute-on-Chronic Liver Failure score. https://efclif.com/research-infrastructure/score-calculators/clif-c-of-aclf-ad/ (access date: 05.06.2025).

[2] Ministry of Health of the Russian Federation. Clinical Guidelines. Liver Cirrhosis and Fibrosis (approved by the Ministry of Health of the Russian Federation, 2022) https://cr.minzdrav.gov.ru/view-cr/715_2 (access date: 05.06.2025).

DISCUSSION

Approximately in 50% of anemia cases observed in patients with liver cirrhosis, as reported by B. Scheiner et al. [1], the underlying etiology remains unknown even after comprehensive laboratory and instrumental diagnostic work up.

The presented clinical case shows the diagnostic workup for anemia, during which all causes of anemia (iron-deficiency, megaloblastic, and hemolytic anemias (including autoimmune anemia and anemia associated with Wilson's disease), as well as anemia due to bone marrow aplasia) were excluded. Based on the combination of clinical, laboratory, and morphological data, a diagnosis of secondary acanthocytosis due to LC was established. Another potential mechanism contributing to anemia could be chronic inflammation in the patient with LC; however, iron metabolism parameters did not indicate functional iron deficiency.

Microscopic examination of the peripheral blood smear revealed diverse red blood cells morphologies: hyperchromic macrocytes, spherocytes, codocytes, echinocytes, acanthocytes, and red blood cells containing Howell–Jolly bodies. This combination may reflect both the severity of the underlying disease and the effects of therapeutic interventions. The presence of spherocytes is likely related to prior blood transfusions, while Howell–Jolly bodies and pronounced poikilocytosis indicate functional hyposplenism developing in LC and during hemolysis [9].

In this case, the absence of hematological pathology prior to liver disease manifestation excludes hereditary forms of acanthocytosis. Normal thyroid-stimulating hormone levels and bone marrow findings ruled out hypothyroidism and myelodysplasia as causes of secondary acanthocytosis.

In routine clinical practice, distinguishing acanthocytes from echinocytes in blood smears may present certain diagnostic challenges. Acanthocytes are pathological, irreversibly altered red blood cells with unevenly distributed spicules, formed due to lipid metabolism disorders, membrane damage from hemolysis, and impaired splenic clearance of defective red blood cells [10]. Echinocytes, by contrast, have evenly distributed projections and are reversible; their appearance may result from osmolarity disturbances, smear preparation technique, or sample transport [11].

SCA in patients with alcoholic LC must be differentiated from Zieve's syndrome, which presents with the triad of hemolysis, jaundice, and dyslipidemia. In Zieve's syndrome, improvement may occur with alcohol cessation and conservative therapy, whereas SCA is irreversible and serves as a marker of poor prognosis [12], as observed in the presented case.

Pharmacotherapy for SCA remains insufficiently studied: few case reports describe positive effects of flunarizine, pentoxifylline, cholestyramine, high-dose steroids, and plasmapheresis [2, 13, 14]. Blood transfusions provide temporary correction but may contribute to iron overload and progression of liver damage.

In the presented patient, the development of ACLF and secondary acanthocytosis were extremely poor prognostic factors. It should be emphasized that among all available interventions, only liver transplantation has demonstrated the ability to reverse both hepatic decompensation and the characteristic red blood cells changes observed in acanthocytosis [15]. This was clearly illustrated by the outcome in our patient.

Given the high prognostic significance of acanthocytosis even in the absence of anemia in patients with ACLF [7], it can be anticipated that this parameter may be evaluated for potential inclusion in future ACLF severity scoring systems.

CONCLUSION

The presented clinical case of SCA highlights the complexity of diagnosing rare causes of anemia in patients with decompensated LC and ACLF. Morphological assessment of peripheral blood smears is a simple and accessible method for detecting acanthocytosis. Liver transplantation remains the only intervention capable of achieving regression of both hepatic insufficiency and acanthocytosis.

AUTHORS CONTRIBUTIONS

Ekaterina O. Liusina, Natalia A. Suvorova and Andrey P. Kostikov participated in the examination, treatment of the patient, literature analysis, preparation of the manuscript text, and critical revision of the manuscript. All the authors approved the final version of the article.

ВКЛАД АВТОРОВ

Е.О. Люсина, Н.А. Суворова и А.П. Костиков принимали участие в проведении обследования, лечения пациента, анализе литературы, подготовке текста рукописи, критическом пересмотре рукописи. Все авторы утвердили окончательную версию статьи.

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INFORMATION ABOUT THE AUTHORS / ИНФОРМАЦИЯ ОБ АВТОРАХ

Ekaterina O. Liusina✉**,** Cand. of Sci. (Medicine), Research Associate, Laboratory of Experimental and Preventive Gastroenterology, National Medical Research Center for Therapy and Preventive Medicine; gastroenterologist, LLC "Chaika White Gardens".
ORCID: https://orcid.org/0000-0001-7640-638X

Natalia A. Suvorova, Cand. of Sci. (Medicine), Associate Professor, Department of Hospital Therapy named after Academician P.E. Lukomsky, Pirogov Russian National Research Medical University; physician, City Clinical Hospital No. 15 named after O.M. Filatov; gastroenterologist, LLC "DOCMED".
ORCID: https://orcid.org/0000-0001-5959-6759

Andrey P. Kostikov, physician, LLC "Children's Clinic".
ORCID: https://orcid.org/0000-0002-1420-8369

Люсина Екатерина Олеговна✉**,** канд. мед. наук, научный сотрудник лаборатории экспериментальной и профилактической гастроэнтерологии ФГБУ «НМИЦ терапии и профилактической медицины» Минздрава России; врач-гастроэнтеролог ООО «Чайка Белые Сады».
ORCID: https://orcid.org/0000-0001-7640-638X

Суворова Наталья Александровна, канд. мед. наук, доцент кафедры госпитальной терапии им. академика П.Е. Лукомского ФГАОУ ВО РНИМУ им. Н.И. Пирогова Минздрава России (Пироговский Университет); врач-терапевт ГБУЗ «ГКБ № 15 ДЗМ»; врач-гастроэнтеролог ООО «ДОКМЕД».
ORCID: https://orcid.org/0000-0001-5959-6759

Костиков Андрей Петрович, терапевт ООО «Детская клиника».
ORCID: https://orcid.org/0000-0002-1420-8369

✉ Corresponding author / Автор, ответственный за переписку

СЕЧЕНОВСКИЙ УНИВЕРСИТЕТ
НАУК О ЖИЗНИ

ФГАОУ ВО «Первый МГМУ им. И.М. Сеченова» Минздрава России
(Сеченовский Университет)