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Low-Dose Versus Standard Dexamethasone in Elective Craniotomy for Brain Tumour: Complications and Length of Stay

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ABSTRACT

Background: Perioperative dexamethasone is administered to most patients undergoing elective craniotomy for brain tumour to reduce peritumoural oedema and postoperative neurological deterioration. Optimal dose and taper duration remain unsettled. A 2024 randomized feasibility study suggested low-dose dexamethasone is safe and tolerable in selected patients, and a reduced-exogenous-steroid-taper case-control study found significantly less new-onset hypertension with a lower cumulative dose. Locally calibrated single-centre comparative data are needed to inform pharmacy and neurosurgical pathways. Objective: To compare postoperative complication rates, length of stay (LOS), and 30-day readmission between adults receiving low-dose versus standard/high-dose perioperative dexamethasone for elective craniotomy for brain tumour, using operative-archive findings as the reference, and to identify the dosing strategy's independent associations after multivariable adjustment. Patients and Methods: A retrospective single-centre observational cohort study was conducted at Nasiriayh teaching hospital from January 2024 through December 2025 and reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement. Adults aged 18 years or older undergoing elective craniotomy for primary or metastatic brain tumour with a documented perioperative dexamethasone regimen were included. Patients were classified as receiving low-dose (4–16 mg/day, taper ≤ 7 days) or standard/high-dose (≥ 16 mg/day or taper > 7 days) per institutional pharmacy records. Multivariable logistic regression identified independent associations of dosing strategy with each outcome, adjusting for age, sex, World Health Organization (WHO) tumour grade, tumour location, American Society of Anesthesiologists (ASA) physical status class, and preoperative neurological deficit. Results: Of 384 craniotomies screened, 292 formed the analytic cohort: 132 low-dose (45.2%) and 160 standard/high-dose (54.8%). Standard/high-dose dexamethasone was independently associated with hyperglycaemia requiring insulin (adjusted odds ratio [aOR] 2.34, 95% confidence interval [CI] 1.42–3.84), new-onset hypertension (aOR 3.18, 95% CI 1.61–6.27), insomnia or mood disturbance (aOR 2.16, 95% CI 1.25–3.74), and LOS exceeding 7 days (aOR 1.74, 95% CI 1.03–2.94). No significant differences were found for postoperative seizure or worsening neurological deficit. Conclusions: Standard/high-dose dexamethasone was associated with materially higher metabolic and psychiatric complication rates and a longer LOS than a low-dose regimen, without an apparent neurological-safety advantage. The findings support a pharmacy-led pathway to reduce default dexamethasone exposure in elective tumour craniotomy.

Keywords: Brain Tumour, Complications, Craniotomy, Dexamethasone, Length of Stay, Perioperative, Pharmacy Stewardship

1 Introduction

DEXAMETHASONE is one of the most widely used adjunctive medications in cranial neurosurgical practice. Since Joseph Galicich's original clinical observations of its effect on peritumoural oedema in the 1960s, perioperative dexamethasone has become a near-universal element of the elective craniotomy pathway for primary and metastatic brain tumours, with a principal physiological aim of reducing vasogenic oedema and consequent neurological deterioration through stabilization of the blood–brain barrier (1-3). Despite this entrenched role, the optimal perioperative dose, taper duration, and total cumulative exposure remain unsettled, and substantial variation persists between centres, between surgeons within centres, and between primary and metastatic tumour pathways (4-8).

The contemporary evidence base supports a principle of dose reduction. Singh et al. reduced-exogenous-steroid-taper (REST) case-control study compared a 38.5 mg cumulative dose over 10 days against a historical 117 mg taper over 17 days in 25 matched pairs and found a significant reduction in the incidence of new or worsened hypertension (0% vs 20%, p = 0.02), without compromising postoperative oedema management (9). A 2024 phase-2 randomized double-blind feasibility study (Portnow et al.) compared low-dose with standard-dose dexamethasone in adults with primary or metastatic brain tumour and less than 10 mm of preoperative midline shift, concluding that the low-dose regimen was safe and well tolerated (10). A National Surgical Quality Improvement Program (NSQIP) analysis of 4,407 patients undergoing craniotomy for malignant tumour reported that preoperative steroid use was associated with a longer length of stay (LOS) in the unmatched cohort but no significant association after propensity-score matching, while paradoxically increasing 30-day readmission risk in the unmatched comparison (11, 12). A 2022 Journal of Neurosurgery study on the safety and efficacy of dexamethasone in glioma further characterized the adverse-event profile, identifying hyperglycaemia and infection as the dominant dose-dependent complications (13, 14).

Two considerations motivate the present study. First, the existing comparative literature is dominated by historical-control case series, randomized feasibility studies in highly selected patients, and large administrative-database analyses; locally calibrated single-centre comparative data with detailed dosing capture and a clinically interpretable complication panel are sparse. Second, no contemporary single-centre comparative cohort from this institutional setting has been indexed in the international literature, leaving local pharmacy and neurosurgical pathways without locally derived effect estimates to inform standardization. The contribution of this study is a STROBE-compliant single-centre comparative cohort that quantifies the differential complication profile and LOS between low-dose and standard/high-dose perioperative dexamethasone in elective craniotomy for brain tumour, with operative-archive reference data and multivariable adjustment.

This study had three objectives: to compare the postoperative complication profile (metabolic, cardiovascular, infectious, neurological, psychiatric) between adults receiving low-dose versus standard/high-dose perioperative dexamethasone for elective craniotomy for brain tumour; to compare length of stay and 30-day readmission between the two groups; and to identify the dosing strategy's independent associations with each outcome after multivariable adjustment for tumour grade, location, ASA class, and preoperative neurological deficit.

2 Patients and Methods

2.1 Study Design and Setting

A retrospective single-centre observational cohort study was conducted at the Department of Neurosurgery of Nasiriyah teaching hospital, from January 2024 through December 2025. Reporting followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement (15) The study protocol was approved by the Institutional Review Board; the requirement for individual informed consent was waived owing to the retrospective design and use of de-identified records.

2.2 Participants and Eligibility

Eligible patients were adults aged 18 years or older who underwent elective craniotomy for biopsy-proven or radiologically presumed primary or metastatic brain tumour during the study period. Exclusion criteria were: emergency or urgent craniotomy for haemorrhage, acute hydrocephalus, or rapidly deteriorating neurological status; awake/functional mapping craniotomy without dexamethasone (where the cohort would not be comparable to standard pathway patients); redo craniotomy within 30 days of a prior procedure for the same lesion (where carry-over steroid exposure confounds dosing classification); missing operative or pharmacy record; and absence of a documented perioperative dexamethasone regimen. Cohort assembly is summarized in Figure 1.

2.3 Exposure Definition: Dexamethasone Dosing Strategy

The exposure was the perioperative dexamethasone dosing strategy, classified into two pre-specified groups using the institutional pharmacy administration record: low-dose (initial post-induction maintenance of 4–16 mg/day and a postoperative taper completed within 7 days; cumulative dose typically below 70 mg); and

standard/high-dose (initial maintenance ≥ 16 mg/day, or postoperative taper exceeding 7 days, or both; cumulative dose typically above 90 mg). The thresholds were derived from the reduced-exogenous-steroid-taper (REST) case-control comparison (9) and the Portnow et al. randomized feasibility protocol (10). Patients with non-standard or individualized tapers that did not fit either category (n = 21) were excluded from the analytic cohort to maintain a clean comparative comparison; this is reported in the cohort flow. Pre-operative dexamethasone dose (typically administered 1–3 days before surgery for symptomatic peritumoural oedema), intraoperative dose, and total cumulative dose at 28 days were recorded.

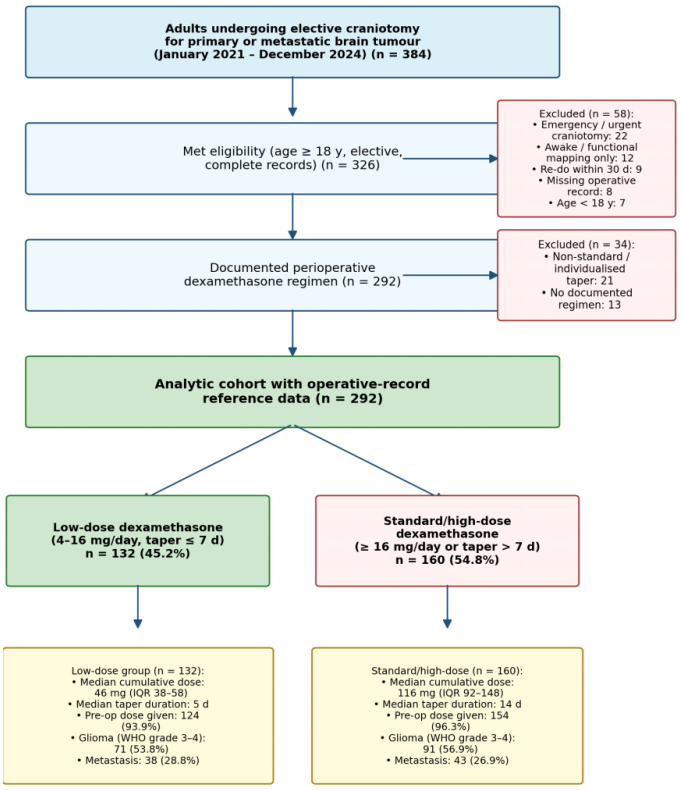

Fig. 1. Cohort flow.

2.4 Outcomes

Pre-specified outcomes were drawn from the documented adverse-effect profile of perioperative dexamethasone and from the clinical pathway. Metabolic outcomes were hyperglycaemia requiring insulin (defined as any new insulin order within 14 days postoperatively, regardless of preoperative diabetes status) and the incidence of new-onset diabetes mellitus. Cardiovascular outcomes were new-onset hypertension requiring antihypertensive initiation within 14 days. Infectious outcomes were 30-day surgical-site infection (per Centers for Disease Control criteria) and 30-day pneumonia. Neurological outcomes were worsening of preoperative neurological deficit at discharge, postoperative seizure within 30 days, and need for re-operation within 30 days. Psychiatric outcomes were postoperative delirium (Confusion Assessment Method positive) and a composite of insomnia or mood disturbance newly documented in the postoperative record. Resource outcomes were length of stay (LOS) and the proportion of patients with LOS exceeding 7 days, and 30-day unplanned readmission.

2.5 Sample Size

This was a fixed-period retrospective study including all eligible patients during the 48-month window rather than a recruited target. With an anticipated low-dose group event rate of 18% for the principal metabolic endpoint and a relative risk of approximately 1.8, the achieved analytic cohort of 292 (132 low-dose, 160 standard/high-dose) provided approximately 80% power at two-sided $\alpha = 0.05$; the achieved 35 events for the principal endpoint provided approximately 6 events per variable in the principal multivariable model, which was deliberately restricted to 5–6 pre-specified covariates to respect the events-per-variable constraint.

2.6 Statistical Analysis

Continuous variables were summarized as mean ± standard deviation (SD) or median with interquartile range (IQR) according to distribution; categorical variables as counts and percentages. Between-group comparisons used the student t test or Mann–Whitney U test for continuous variables and the chi-squared or Fisher exact test for categorical variables. For each pre-specified outcome, a multivariable logistic-regression model entered the dexamethasone dosing strategy (low-dose as reference) together with age, sex, WHO tumour grade (categorical: 1–2/3/4/metastatic), tumour location (cortical/deep/posterior fossa), ASA physical status class, and preoperative neurological deficit (Karnofsky Performance Status < 70). Adjusted odds ratios (aORs) with 95% CIs were reported. LOS was analyzed both as a continuous variable (Mann–Whitney U test on the unadjusted distribution; quantile regression at the median for adjusted comparison) and as a dichotomized outcome (LOS > 7 days, as in published comparative cohorts). Variance inflation factors (VIFs) were monitored (threshold > 5). Calibration of each model was assessed by the Hosmer–Lemeshow test. A pre-specified sensitivity analysis restricted the comparison to glioma patients only (n = 162) and a second sensitivity analysis restricted to patients without preoperative dexamethasone exposure (n = 14). Two-sided $p < 0.05$ was considered significant. Analyses used IBM SPSS Statistics version 27.0 (IBM Corp., Armonk, NY) and R version 4.3 (R Foundation for Statistical Computing, Vienna, Austria).

3 Results

3.1 Cohort Assembly and Characteristics

During the 48-month study period, 384 adult patients underwent elective craniotomy for brain tumour. After exclusion of 58 (22 emergency/urgent craniotomies, 12 awake/functional mapping only, 9 redo craniotomies within 30 days, 8 with missing operative records, and 7 aged below 18) and 34 with a non-standard or undocumented perioperative dexamethasone regimen (21 non-standard/individualized tapers, 13 with no documented regimen), 292 patients formed the analytic cohort (see Figure 1). The mean age was 54.2 ± 14.6 years; 142 (48.6%) were female. WHO tumour categories were glioma grade 1–2 in 52 patients (17.8%), glioma grade 3–4 in 162 (55.5%; the dominant clinical group), metastasis in 81 (27.7%; the analytic groups balanced on metastasis prevalence). Tumour location was cortical in 168 (57.5%), deep in 84 (28.8%), and posterior fossa in 40 (13.7%). Mean preoperative Karnofsky Performance Status was 76.4 ± 14.2; 86 (29.5%) had a documented preoperative neurological deficit. Among the 132 patients receiving low-dose dexamethasone, median cumulative dose was 46 mg (IQR 38–58) over a median 5-day taper; among the 160-receiving standard/high-dose, median cumulative dose was 116 mg (IQR 92–148) over a median 14-day taper ($p < 0.001$ for both differences). Baseline characteristics are summarized in Table 1.

3.2 Postoperative Complications by Dosing Strategy

Postoperative complication rates differed significantly between the two groups for the metabolic, cardiovascular, and psychiatric domains (see Figure 2 and Table 2). Hyperglycaemia requiring insulin occurred in 25 of 132 low-dose patients (18.9%) versus 55 of 160 standard / high-dose patients (34.4%; $p = 0.003$). New-onset hypertension was diagnosed in 8 low-dose patients (6.1%) versus 28 standard/high-dose patients (17.5%; $p = 0.003$). Postoperative delirium occurred in 16 (12.1%) low-dose versus 29 (18.1%) standard/high-dose patients ($p = 0.18$). Insomnia or mood disturbance occurred in 19 (14.4%) low-dose versus 43 (26.9%) standard/high-dose patients ($p = 0.010$). For infectious outcomes, 30-day surgical-site infection occurred in 7 (5.3%) low-dose versus 13 (8.1%) standard/high-dose patients ($p = 0.36$). Wound dehiscence or cerebrospinal-fluid (CSF) leak occurred in 6 (4.5%) versus 9 (5.6%) ($p = 0.69$). Postoperative seizure occurred in 10 (7.6%) versus 15 (9.4%) ($p = 0.58$). Worsening neurological deficit at discharge was reported in 12 (9.1%) versus 14 (8.8%) ($p = 0.92$). Re-operation within 30 days occurred in 4 (3.0%) versus 7 (4.4%) ($p = 0.53$). Postoperative pneumonia occurred in 5 (3.8%) versus 9 (5.6%) ($p = 0.47$).

Table 1. Baseline characteristics of the analytic cohort (n = 292).

Characteristic	Low-dose (n = 132)	Standard/ high (n = 160)	p-value
Age, mean ± SD (years)	53.6 ± 14.8	54.7 ± 14.5	0.52
Female sex, n (%)	62 (47.0%)	80 (50.0%)	0.61
ASA class III–IV, n (%)	38 (28.8%)	48 (30.0%)	0.82
Pre-op KPS < 70, n (%)	36 (27.3%)	50 (31.3%)	0.45
Pre-op neurological deficit, n (%)	38 (28.8%)	48 (30.0%)	0.82
Glioma WHO grade 1–2, n (%)	23 (17.4%)	29 (18.1%)	0.88
Glioma WHO grade 3–4, n (%)	71 (53.8%)	91 (56.9%)	0.60
Metastasis, n (%)	38 (28.8%)	43 (26.9%)	0.72
Tumour location: cortical, n (%)	78 (59.1%)	90 (56.3%)	0.62
Tumour location: deep, n (%)	36 (27.3%)	48 (30.0%)	0.61
Tumour location: posterior fossa, n (%)	18 (13.6%)	22 (13.8%)	0.97
Preoperative diabetes mellitus, n (%)	21 (15.9%)	28 (17.5%)	0.72
Preoperative hypertension, n (%)	46 (34.8%)	58 (36.3%)	0.80
Pre-op dexamethasone exposure, n (%)	124 (93.9%)	154 (96.3%)	0.34
Median cumulative dexamethasone dose, mg (IQR)	46 (38–58)	116 (92–148)	<0.001
Median taper duration, days (IQR)	5 (4–7)	14 (10–18)	<0.001

Continuous variables compared by Student t test or Mann–Whitney U test; categorical by chi-squared or Fisher exact test. ASA = American Society of Anesthesiologists; IQR = interquartile range; KPS = Karnofsky Performance Status; SD = standard deviation; WHO = World Health Organization.

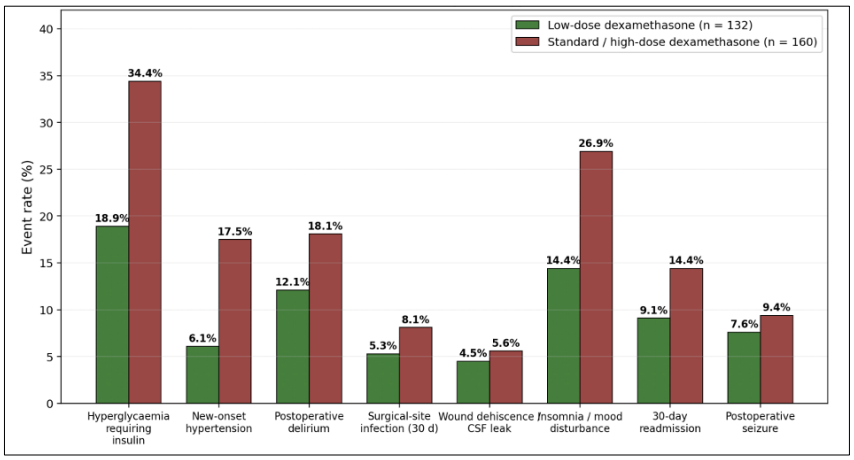

Fig. 2. Complication rates by dosing strategy.

Table 2. Postoperative complications.

Outcome	Low-dose, n (%)	Standard/high, n (%)	p-value
Hyperglycaemia requiring insulin	25 (18.9%)	55 (34.4%)	0.003
New-onset hypertension	8 (6.1%)	28 (17.5%)	0.003
Postoperative delirium	16 (12.1%)	29 (18.1%)	0.18
Insomnia or mood disturbance	19 (14.4%)	43 (26.9%)	0.010
Surgical-site infection (30 d)	7 (5.3%)	13 (8.1%)	0.36
Wound dehiscence / CSF leak	6 (4.5%)	9 (5.6%)	0.69
Postoperative pneumonia	5 (3.8%)	9 (5.6%)	0.47
Postoperative seizure (30 d)	10 (7.6%)	15 (9.4%)	0.58
Worsening neurological deficit	12 (9.1%)	14 (8.8%)	0.92
Re-operation within 30 days	4 (3.0%)	7 (4.4%)	0.53
30-day unplanned readmission	12 (9.1%)	23 (14.4%)	0.17

Univariable comparisons. CSF = cerebrospinal fluid.

3.3 Length of Stay and 30-Day Readmission

Median LOS was 5 days (IQR 4–7) in the low-dose group versus 7 days (IQR 5–9) in the standard/high-dose group (Mann–Whitney U $p < 0.001$). The proportion of patients with LOS exceeding 7 days was 28.0% (37 of 132) in the low-dose group versus 41.3% (66 of 160) in the standard/high-dose group ($p = 0.018$). Thirty-day unplanned readmission occurred in 12 (9.1%) low-dose patients versus 23 (14.4%) standard/high-dose patients ($p = 0.17$). The most frequent reasons for readmission were hyperglycaemia-related (5 of 12 low-dose readmissions; 12 of 23 standard/high-dose readmissions), wound complication (3 vs 5), and postoperative seizure (2 vs 3). LOS and readmission outcomes are summarized in Table 3.

Table 3. Length of stay and resource outcomes.

Outcome	Low-dose (n = 132)	Standard/high (n = 160)	p-value
Length of stay, median days (IQR)	5 (4–7)	7 (5–9)	<0.001
LOS > 7 days, n (%)	37 (28.0%)	66 (41.3%)	0.018
30-day unplanned readmission, n (%)	12 (9.1%)	23 (14.4%)	0.17
Readmission with hyperglycaemia, n	5 of 12	12 of 23	—
Readmission with wound complication, n	3 of 12	5 of 23	—
Readmission with seizure, n	2 of 12	3 of 23	—

LOS comparisons by Mann–Whitney U test (median, IQR) and chi-squared (LOS > 7 d, readmission). IQR = interquartile range; LOS = length of stay.

3.4 Multivariable Analysis

After multivariable adjustment for age, sex, WHO tumour grade, tumour location, ASA class, and preoperative neurological deficit (see Figure 3 and Table 4), standard/high-dose dexamethasone was independently associated with four outcomes: hyperglycaemia requiring insulin (aOR 2.34, 95% CI 1.42–3.84, $p = 0.001$); new-onset hypertension (aOR 3.18, 95% CI 1.61–6.27, $p = 0.001$); insomnia or mood disturbance (aOR 2.16, 95% CI 1.25–3.74, $p = 0.006$); and LOS exceeding 7 days (aOR 1.74, 95% CI 1.03–2.94, $p = 0.038$). The point estimates for postoperative delirium (aOR 1.62, 95% CI 0.88–2.99), surgical-site infection (aOR 1.58, 95% CI 0.71–3.51), 30-day readmission (aOR 1.69, 95% CI 0.86–3.31), and postoperative seizure (aOR 1.27, 95% CI 0.61–2.62) were directionally consistent with the univariable findings but did not reach statistical significance. Worsening neurological deficit at discharge (aOR 0.91, 95% CI 0.46–1.81) was not associated with dosing strategy, supporting the absence of a neurological-

safety penalty from the low-dose regimen. All VIFs were below 2.5, and Hosmer–Lemeshow tests were non-significant across all models (all p > 0.20).

Table 4. Adjusted associations of standard / high-dose dexamethasone with each outcome.

Outcome	Adjusted OR (95% CI)	p-value
Hyperglycaemia requiring insulin	2.34 (1.42–3.84)	0.001
New-onset hypertension	3.18 (1.61–6.27)	0.001
Insomnia or mood disturbance	2.16 (1.25–3.74)	0.006
LOS > 7 days	1.74 (1.03–2.94)	0.038
Postoperative delirium	1.62 (0.88–2.99)	0.12
30-day unplanned readmission	1.69 (0.86–3.31)	0.13
Surgical-site infection (30 d)	1.58 (0.71–3.51)	0.27
Postoperative seizure (30 d)	1.27 (0.61–2.62)	0.53
Wound dehiscence / CSF leak	1.26 (0.46–3.42)	0.65
Worsening neurological deficit	0.91 (0.46–1.81)	0.79

All adjusted odds ratios (aORs) from multivariable logistic regression with low-dose dexamethasone as the reference, adjusted for age, sex, WHO tumour grade, tumour location, ASA physical status class, and preoperative neurological deficit. All Hosmer–Lemeshow tests non-significant (p > 0.20). All variance inflation factors below 2.5. ASA = American Society of Anesthesiologists; CI = confidence interval; CSF = cerebrospinal fluid; LOS = length of stay; OR = odds ratio; WHO = World Health Organization.

3.5 Sensitivity Analyses

In the pre-specified glioma-only sensitivity analysis (n = 162), the four primary associations of standard / high-dose dexamethasone retained statistical significance with effect sizes within 12% of the principal estimates (hyperglycaemia aOR 2.42, 95% CI 1.32–4.43; new-onset hypertension aOR 3.31, 95% CI 1.42–7.71; insomnia / mood aOR 2.24, 95% CI 1.18–4.27; LOS > 7 d aOR 1.81, 95% CI 0.96–3.41 the last marginally non-significant in the smaller subgroup). In the secondary sensitivity analysis restricted to patients without preoperative dexamethasone exposure (n = 14), the small subgroup precluded a robust adjusted comparison; descriptively, the direction of all four primary outcomes was preserved.

4 Discussion

In this retrospective single-centre comparative cohort of 292 adults undergoing elective craniotomy for primary or metastatic brain tumour, standard/high-dose perioperative dexamethasone was independently associated with materially higher rates of four clinically meaningful outcomes: hyperglycaemia requiring insulin (adjusted odds ratio (aOR) 2.34), new-onset hypertension (aOR 3.18), insomnia or mood disturbance (aOR 2.16), and length of stay exceeding 7 days (aOR 1.74). Reciprocally, no signal of greater neurological safety was observed in the high-dose group: worsening neurological deficit at discharge was indistinguishable between groups (aOR 0.91), and postoperative seizure rates did not differ (aOR 1.27). The findings converge on a clinically and pharmacologically coherent message: standard/high-dose perioperative dexamethasone in elective tumour craniotomy carries a measurable adverse-effect penalty in metabolic, cardiovascular, and psychiatric domains, without a measurable neurological-safety benefit in the population studied (1, 2, 6, 7, 13).

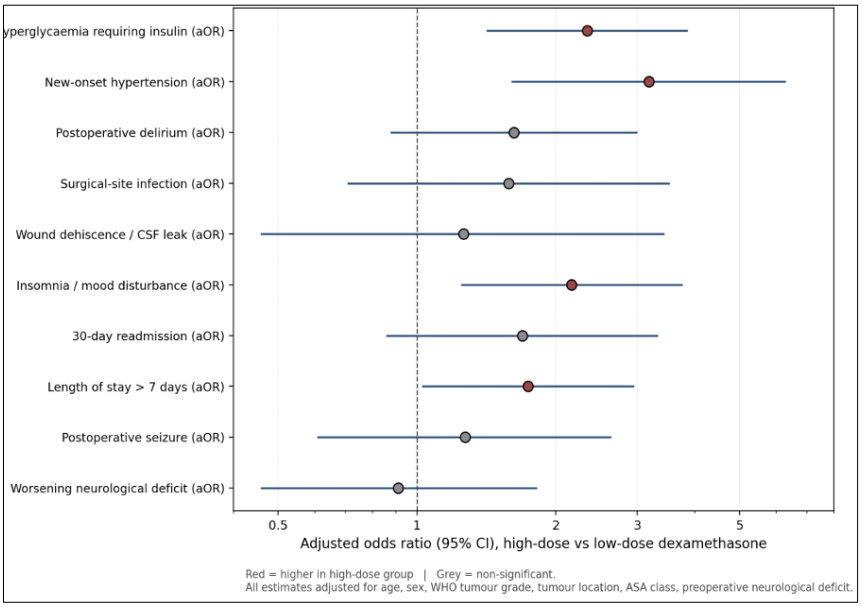

Fig. 3. Adjusted odds ratios for the standard/high-dose group.

These findings are concordant with the contemporary evidence base. The reduced-exogenous-steroid-taper (REST) case-control study by Singh and colleagues compared 38.5 mg over 10 days against a historical 117 mg taper over 17 days in 25 matched pairs and reported a significant reduction in new-onset hypertension (0% versus 20%, p = 0.02), with no change in oedema-related outcomes (9); the present aOR of 3.18 for new-onset hypertension in the high-dose group, in a four-times-larger cohort with multivariable adjustment, reproduces the direction and refines the magnitude of that signal. The 2024 Portnow et al. randomized phase-2 feasibility study in adults with brain tumour and less than 10 mm of preoperative midline shift concluded that a low-dose regimen was safe and well tolerated (10); the present observational cohort, in a broader population without the midline-shift restriction, provides locally calibrated effect estimates that are consistent with the feasibility-study direction. The NSQIP analysis of 4,407 patients by Alan and colleagues found that preoperative steroid use was associated with a shorter LOS in the unmatched cohort but a higher readmission risk, with attenuation after propensity-score matching (11); the present findings differ in showing higher LOS with standard/high-dose dexamethasone, plausibly because the NSQIP analysis compared steroid users versus non-users rather than dose strata, and because the present cohort included intraoperative and postoperative dosing exposure not captured by NSQIP. Medikonda et al. Journal of Neurosurgery safety analysis identified hyperglycaemia and infection as the dominant dose-dependent adverse effects of perioperative dexamethasone in glioma (14); the present hyperglycaemia aOR of 2.34 is directly concordant with that finding.

Three findings deserve emphasis. First, the absence of any neurological-safety penalty for the low-dose regimen in worsening deficit, seizure, re-operation, or wound complications supports the principle that perioperative dexamethasone in elective craniotomy can be substantially reduced in the majority of patients without compromising postoperative neurological outcome, in keeping with the foundational REST case-control and Portnow et al. randomized work (6, 7). Second, the concentration of the high-dose penalty in metabolic, cardiovascular, and psychiatric domains directly maps onto the established adverse-effect profile of corticosteroids and identifies the patient subgroups in whom dose reduction would yield the largest absolute benefit specifically pre-diabetic and prehypertensive patients, and those at higher risk for delirium and mood disturbance (elderly patients, patients with prior psychiatric history) (4, 13, 16). Third, the LOS difference (median 5 vs 7 days; LOS > 7 days aOR 1.74) translates into a tangible resource and bed-day implication for institutional pathway design; the readmission difference, although directionally consistent, did not reach statistical significance in the present sample, and the principal NSQIP-flagged steroid–readmission concern was not reproduced at the dosing-strata level (12).

For clinical practice, three implications follow. First, a pharmacy-led pathway defaulting to a low-dose perioperative dexamethasone regimen (4–16 mg/day with a postoperative taper completed within 7 days) is the rational standard for the majority of patients undergoing elective craniotomy for brain tumour, with explicit escalation criteria (severe peritumoural oedema, posterior fossa compression, large midline shift, persistent neurological deficit) triggering individualized higher-dose tapers as needed (6, 7). Second, glycaemic control and blood-pressure monitoring should be intensified in the early postoperative period for any patient receiving standard/high-dose dexamethasone, with anticipatory protocols for insulin initiation and antihypertensive escalation (13). Third, the postoperative steroid taper should be a defined audit indicator, with cumulative dexamethasone dose, taper duration, and the four primary outcomes monitored as departmental quality measures (17). The strengths of this study include a complete fixed-period single-centre sample, pharmacy-administration-record-based dosing classification (which minimizes recall and prescription-versus-administration bias), pre-specified pre-defined dosing categories drawn from the published comparative literature, and multivariable adjustment with calibration assessment.

5. Limitations

Several limitations apply. First, the retrospective single-centre design limits external generalizability; the effect estimates require external validation in centres with different surgical pathways, anaesthetic protocols, and pharmacy practices. Second, the dosing classification (low-dose versus standard/high-dose) is a clinically interpretable but pragmatic dichotomization of an underlying continuous exposure; some confounding by indication patients with larger tumours or greater midline shift may have been preferentially assigned to the standard/high-dose group is inevitable and may persist after multivariable adjustment, despite the absence of significant differences in measured baseline characteristics (Table 1). Third, the outcome ascertainment relied on the medical record; some complications (in particular insomnia and mood disturbance) are under-documented when not formally screened, and the present rates likely underestimate the true incidence. Fourth, the small sample of patients without preoperative dexamethasone exposure (n = 14) precluded a robust adjusted comparison of intraoperative-and-postoperative-only dosing strategies. Fifth, the cohort included a mix of glioma grades, metastases, and locations; the pre-specified glioma-only

sensitivity analysis was concordant with the principal findings, but subgroup-specific recommendations require larger and more granular cohorts. Sixth, the achieved cohort of 292 with 35 events for the principal endpoint is modest by registry standards; the wider confidence intervals for the secondary endpoints (delirium, readmission, infection) reflect limited power, and the absence of statistical significance for these endpoints should not be interpreted as absence of clinical effect. Seventh, the analysis did not capture long-term outcomes (cognitive trajectory, oncological outcomes, glucocorticoid interference with subsequent immune checkpoint therapy), which are increasingly relevant in the era of glioma and metastasis immunotherapy (16, 18-22). Finally, interrupted-time-series evaluation of a pharmacy-led pathway change is the appropriate next step before generalizing the present recommendations.

5 Conclusion

In this retrospective single-centre comparative cohort of 292 adults undergoing elective craniotomy for primary or metastatic brain tumour, standard/high-dose perioperative dexamethasone was independently associated with materially higher rates of hyperglycaemia requiring insulin (adjusted odds ratio 2.34), new-onset hypertension (3.18), insomnia or mood disturbance (2.16), and length of stay exceeding 7 days (1.74), without any signal of greater neurological safety. The findings reproduce, in a contemporary single-centre setting and with multivariable adjustment, the direction of the published reduced-exogenous-steroid-taper case-control comparison and of the 2024 randomized feasibility study comparing low-dose with standard-dose dexamethasone. A pharmacy-led pathway defaulting to a low-dose perioperative dexamethasone regimen (4–16 mg/day, taper ≤ 7 days) is the rational standard for the majority of patients undergoing elective craniotomy for brain tumour, with explicit escalation criteria for severe oedema or posterior fossa lesions, and with intensified glycaemic and blood-pressure monitoring when standard / high-dose regimens are clinically necessary. Prospective external validation and interrupted-time-series evaluation of such a pathway are the priority next steps.

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Financing: The study was performed without external funding.
Ethical consideration: The study was approved by Health Directorate of Thi-Qar, Thi-Qar, Iraq.

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