NEUROSURGICAL FOCUS

Neurosurg Focus 55(6):E9, 2023

# The Enhanced Recovery After Surgery protocol for the perioperative management of pituitary neuroendocrine tumors/pituitary adenomas

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**OBJECTIVE** Enhanced Recovery After Surgery (ERAS) is a multimodal perioperative care pathway that has radically modified the management of patients in multiple surgical specialties. Until now, no ERAS Society guidelines have been formulated for the management of cranial pathologies. During the process of ERAS certification for their neurosurgical department, the authors formulated an ERAS protocol for the perioperative care of patients with pituitary neuroendocrine tumors (PitNET), along with a compliance checklist to monitor the adherence to it and its feasibility. The authors describe the protocol and checklist and report the results, including a cost-minimization analysis, with the application of the ERAS philosophy.

**METHODS** The steps that led to the development of this ERAS protocol, including items concerning the preoperative, intraoperative, and postoperative period, are detailed. The authors report their preliminary results through the comparison of the care practice of a historical cohort with a consecutive surgical cohort of patients with PitNET who underwent operation after the implementation of this ERAS protocol. A compliance checklist with key performance indicators was useful to monitor the adherence to the protocol and the changes in the perioperative management.

**RESULTS** Following the introduction of this ERAS protocol, the authors significantly shortened the duration of the antibiotic therapy ($p < 0.00001$) and increased the use of mechanical ($p < 0.00001$) and pharmacological measures to prevent deep venous thrombosis ($p = 0.002$). The median length of hospital stay was significantly shorter for the ERAS group ($p = 0.00014$), and there was no increase in readmission rate or postoperative complications. The documentation and data tracking strongly improved in the ERAS cohort and the authors were more attentive in pain evaluation ($p = 0.001$), postoperative hormonal supplementation ($p = 0.001$) and early feeding and mobilization ($p = 0.0008$ and $p < 0.00001$, respectively). More patients were discharged on day 3 after surgery in the ERAS group ($p < 0.00001$). The compliance to the whole process increased from 64.2% to 89.5% ($p = 0.016$), and the compliance per patient was also found to have significantly increased ($p < 0.00001$).

**CONCLUSIONS** The introduction of a standardized ERAS protocol for the perioperative management of patients with PitNET allowed the authors to improve the multidisciplinary management of these patients. With the application of simple cost-effective interventions and with the avoidance of unnecessary measures, gains were made in terms of early mobilization and feeding, thereby resulting in a shorter in-hospital stay.

https://thejns.org/doi/abs/10.3171/2023.9.FOCUS23529

**KEYWORDS** ERAS; Enhanced Recovery After Surgery; endoscopy; PitNET; pituitary neuroendocrine tumors; pituitary adenoma; surgery; management

**ABBREVIATIONS** ACTH = adrenocorticotropic hormone; CHF = Confederatio Helvetica francs; DI = diabetes insipidus; DVT = deep venous thrombosis; ERAS = Enhanced Recovery After Surgery; ICA = internal carotid artery; IMCU = intermediate care unit; IV = intravenous; LOS = length of hospital stay; PitNET = pituitary neuroendocrine tumors.

**SUBMITTED** July 30, 2023. **ACCEPTED** September 28, 2023.
**INCLUDE WHEN CITING** DOI: 10.3171/2023.9.FOCUS23529.

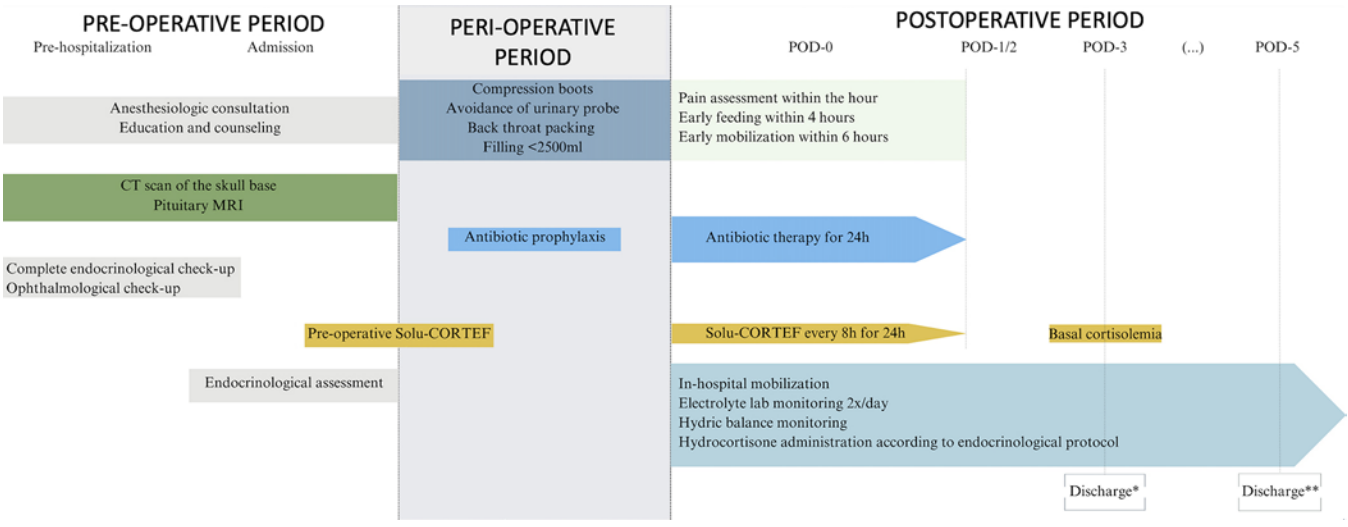


**FIG. 1.** The interventions are graphically represented. *Arrows* represent repeated interventions according to the defined timeline. Discharge criteria on day 3 (*) or 5 (**) after surgery are defined in the text according to patient age and physical condition, presence of postoperative complications, and pathology. POD = postoperative day.

ENDOSCOPIC transsphenoidal surgery represents the gold standard for the management of pituitary neuroendocrine tumors (PitNET) for the last 2 decades.[1–4] The well-known complications related to the surgical management of these patients include new postoperative pituitary insufficiencies, visual worsening, and CSF leakage, along with vascular injuries, with a possible impact on the quality of life of our patients.[5] Minor local and systemic complications, such as rhinitis or sinusitis, urinary retention/infection, or deep venous thrombosis (DVT), remain underreported. However, these complications can have a large impact on the management of our patients as well as on the length of hospital stay (LOS) and costs.

Enhanced Recovery After Surgery (ERAS) is a multimodal perioperative care pathway that has radically modified the management of patients in multiple surgical specialties.[6–13] ERAS Society guidelines target perioperative stress with specific goal-directed evidence-based practices,[7–9,11,14–16] to obtain faster healing, a reduction in complications, and lower readmission and reintervention rates and thus a shorter in-hospital stay with diminished overall costs.[14,15,17–21]

Different neurosurgical centers introduced ERAS protocols in the management of their patients,[22–30] and despite their encouraging results there are not yet any official guidelines from the ERAS Society dealing with the perioperative care of cranial procedures.

At the University Hospital of Lausanne, we obtained certification for our neurosurgical department from the ERAS Society in June 2023, after a process lasting 14 months. During this period, four seminars were followed with three working periods between the seminars dedicated to the construction of our ERAS protocol to define the perioperative care of patients with PitNET and our compliance criteria, to monitor and obtain feedback about the application of this protocol. A multidisciplinary team was instituted, including neurosurgeons, endocrinologists, ophthalmologists, anesthesiologists, and an ERAS-certified nurse dedicated to the elaboration of this protocol (Supplemental Fig. 1), of a clinical itinerary to guide the clinical practice (Supplemental Fig. 2), as well as of a patient booklet (Supplemental Fig. 3) to maximize patients' knowledge of and compliance with the process.

The aim of this paper was to describe our ERAS protocol for the perioperative care of PitNET, along with the chosen criteria of compliance, that represent the key points to determine the adherence to the protocol and to support the feasibility of the protocol itself. We also present our preliminary results in a surgical cohort of patients with PitNET who were consecutively enrolled after the introduction of our local ERAS protocol and who were compared to a historical consecutive cohort.

## Methods

### Protocol Redaction

Based on other ERAS guidelines,[6,11,18,31,32] our protocol included three phases, as follows: 1) the preoperative management, including a preadmission phase along with a postadmission phase before surgery; 2) the perioperative phase; and 3) the postoperative phase.

The different interventions included in every phase are summarized in Fig. 1 and detailed in Supplemental Figs. 1 and 2. A literature review was performed concerning the different aspects of the protocol by the members of the multidisciplinary group, to assess current evidence regarding the best clinical practice in the perioperative management of our patients.

### Preoperative Phase

The preparation work starts already during the preoperative phase. A neurosurgical consultation is performed to explain the surgical procedure along with the reconstructive plan and the perioperative management. A preoperative education and counseling session is performed

by the ERAS nurse in a dedicated consultation. We educate patients about the harmful effects of smoking and alcohol, but abstinence is not considered as an essential factor in their management, because surgery is often organized 2–3 weeks after the consultation and the standard 4-week period of abstinence for smoking asked by ERAS protocols in other specialties[20,33] could not be respected. A patient booklet is also provided to support the discussion (Supplemental Fig. 3). An endocrinological examination is performed in the outpatient clinic and repeated the day before surgery to prepare the patient for the possible hormonal insufficiencies and their respective management.

During the anesthesiology consultation, the anesthesiological procedure is detailed and patients' medications can be optimized.

### Perioperative Phase

During the perioperative phase, a standard anesthetic protocol is applied, with the aim of avoiding unnecessary invasive monitoring. Intravenous (IV) hydrocortisone (Solu-CORTEF—except for patients with Cushing's disease) and antibiotic therapy should be administered according to the protocol at 60 minutes and 20 minutes, respectively, before starting the surgical procedure. Other forms of glucocorticoids should be avoided to limit interference with the postoperative cortisol measurement. Sedating premedication is avoided. Clear fluids are allowed until 2 hours before surgery. An arterial line is reserved for patients with acromegaly, Cushing's disease, or with a clear invasion of the cavernous sinus. A urinary catheter is only considered if the surgery is expected to last more than 3 hours, such as for large or giant tumors or for tumors showing an invasion of the subarachnoid space. To facilitate the detection of postoperative diabetes insipidus (DI), we limit fluid intake to 2500 ml if the surgery lasts less than 4 hours. Prophylaxis against nausea and vomiting is administered early during surgery.

Concerning the operative technique, the patient is positioned with the head elevated at 30° to lower venous pressure and limit the bleeding. We use an endoscopic uninostril approach to limit damage to the contralateral nasal mucosa,[34] and we perform the procedure under neuroimaging-guided navigation. Binostril access is reserved for large or giant tumors.[35] Throat packing material is put in place at the beginning of the procedure to avoid blood leakage into the gastrointestinal tract. We avoid the use of lumbar drains for PitNET surgery and the reconstruction for arachnoid tears is performed with autologous abdominal fat and glue, with no nasoseptal flap. This limits the risks associated with the use of lumbar drains and of immobilization. No nasal packing is performed at the end of the procedure, to allow patients to breath as quickly as possible through the nose. Gentle awakening is a key factor to avoid coughing or the Valsalva maneuver and thus minimize the risk of CSF leakage in the postoperative period.

### Postoperative Phase

The key factors of the postoperative phase are as follows: 1) optimal pain control while limiting morphine and its derivatives; 2) nausea and vomiting prevention; 3) early mobilization within 6 hours from the end of the surgical procedure, and then progressive mobilization during the following days until discharge; and 4) early oral hydration and feeding within 4 hours from the end of surgery. A strict protocol for hydrocortisone and antibiotic therapy administration is established. The discharge decision from the intermediate care unit (IMCU) is based on hemodynamic stability, absence of fever, resumption of adequate mobilization, and pain control.

After surgery, patients were regularly monitored for polyuria-polydipsia symptoms and fluid balance. Serum/urine sodium and osmolality were systematically measured twice daily as well as in case of any new-onset polyuria. The latter was defined as a consistently increased urinary flow (> 300 ml per hour or 4 ml/kg for over- or underweight subjects) in the last 2–3 hours.

The diagnosis of DI was made if the polyuria was hypotonic (inappropriately low urine osmolality for serum osmolality) and was accompanied by hypernatremia or high-normal sodium levels (> 142 mmol/L).[36] Alternative diagnoses such as hyperglycemia, excessive fluid administration, or transient natriuresis postremission in acromegaly were considered before reaching the DI diagnosis. Patients were then treated with oral or IV fluids as well as a desmopressin bolus orally (0.1–0.2 mg) or sublingually (60–120 μg). IV administration (0.5–2 μg) was preferred in patients with decreased consciousness or other issues preventing oral intake. Serum electrolyte and urine osmolality were rechecked after 2–4 hours to confirm adequate pharmacological response. If several doses were required before the discharge, a fixed administration of desmopressin was prescribed at home.

Discharge from hospital was set at 3 days after surgery after basal cortisol dosage if the patient met the following criteria: 1) was < 75 years old and in good physical condition; 2) had an uncontrolled DI; 3) showed no CSF leakage; 4) had no fever or other surgical complications; 5) did not have an adrenocorticotropic hormone (ACTH)–secreting PitNET (all the other PitNET subtypes are included here); and 6) was capable of adjusting their cortisol treatment on their own (stress dosage).

Discharge from hospital was set at 5 days after surgery if the patient was not fulfilling criteria for discharge on day 3. The occurrence of DI did not preclude a hospital discharge at day 3, provided that the patient's symptoms were controlled with treatment, electrolyte levels were normal, and an early outpatient reassessment after 2–3 days was feasible.

Monitoring of pituitary functions continued after discharge from the hospital, with hormone and electrolyte blood tests performed at the outpatient clinic. We created a structure with contact points for patients and families in case of problems after discharge. A smartphone application was used (CHUV@home) to perform health surveys twice per day during the first week and was able to detect the most common complications, namely DI, rhinoliquorrhea, epistaxis, or new vision deficits. In case a complication was suspected, a team of trained nurses promptly contacted the patient, and the medical team was also notified to manage the case. Additionally, our ERAS nurse proactively reached out to all patients 10–14 days after surgery

**TABLE 1. List of the items screened in the pre-, intra-, and postoperative period**

| Preop Phase | Periop Phase | Postop Phase |
|---|---|---|
| Anesthesiology consultation | Compression boots | 24-hr postop antibiotic therapy |
| Preop education & counseling | Prophylactic antibiotic therapy | Postop IV hydrocortisone (Solu-CORTEF) every 8 hrs |
| Endocrinological checkup | Avoidance of urinary probe during surgery | Pain evaluation in 1st hr postsurgery |
| Ophthalmological checkup | Throat packing | Early feeding during the 4 hrs after surgery |
| CT scan | Intraop hydration <2500 ml | Early mobilization w/in 6 hrs |
| Pituitary MRI | | In-hospital mobilization |
| Endocrinology consultation the day before surgery | | Electrolyte controls 2×/day |
| Preop IV hydrocortisone (Solu-CORTEF) in the hr before surgery | | Hydric balance |
| | | Hydrocortisone administration according to endocrinological protocol |
| | | Basal cortisolemia on POD3 |
| | | Discharge on POD3* |
| | | Discharge on POD5† |

POD = postoperative day.
Items represent key markers of compliance with the ERAS protocol, and adherence to these items was continuously assessed.
* After basal cortisol dosage and if the following criteria were fulfilled: patients < 75 years old and in good physical condition; no DI or controlled DI (patient's symptoms controlled with medications and normal electrolyte levels); no CSF leakage; no fever or other surgical complications; lesion was not an ACTH-secreting PitNET; and patients capable of adapting their cortisol treatment on their own (stress dosage).
† For all patients not fulfilling criteria for discharge on day 3 after surgery.

to assess their clinical status and address any concerns they may have had.

### Checklist

A checklist was developed to include performance indicators and evaluate the compliance with the protocol (Table 1). This document was used to assess the feasibility of the protocol along with our adherence to the different criteria. For each indicator, the percentage of compliance was calculated as the fraction of the number of patients compliant with the criterion over the number of patients included. Missing data were recorded as due to noncompliance. On the model of other ERAS protocols, we defined compliance with a criterion as when it was respected in at least 70% of patients consecutively analyzed. We also calculated compliance per patient; i.e., the number of criteria in which the patient was complying with the ERAS protocol over the total number of criteria. This enables us to study whether patients overall turn out to be more compliant with the ERAS protocol after its introduction. The rate of compliance with the protocol in its entirety per patient is the average protocol compliance per patient.

To maximize adherence to our protocol, an information session was organized for the medical and the nurse teams to familiarize and train them in the application of this protocol.

### Data Collection

A prospectively collected database on REDCap was used to perform a retrospective review of consecutively surgically treated cases of PitNET. The use of the ENCARE program, which is the official program of the ERAS Society, was not possible at this stage because no official guidelines had been established yet. We included 30 cases in the pre-ERAS cohort, consecutively surgically treated between December 2018 and December 2019. We included 31 cases in the ERAS cohort that was surgically treated between September 2022 and June 2023.

Functioning and nonfunctioning micro- and macro-PitNET were included. Emergency cases were excluded because they could not undergo an adequate preoperative education and counseling.

Costs of the stay were obtained using a microcosting approach,[37] and included all costs attributed to resource consumption during the hospital stay.

### Outcomes and Statistics

We performed a quality control assessment of our protocol through the analysis of our compliance with the checklist criteria before (pre-ERAS cohort) and after the introduction of our protocol (ERAS cohort). We compared whether our protocol had a positive impact on the management of our patients, namely on the LOS at the IMCU and on the total LOS. We also analyzed if we had an impact on other factors such as pain, nausea, and vomiting management; complications; and 30-day readmission rates. The study was approved by our local ethics committee.

Postoperative complications were classified according to the Clavien-Dindo classification.[38]

Descriptive statistics were used to compare patients' baseline characteristics. The Pearson chi-square test was used to assess homogeneity of the two cohorts. The Kolmogorov-Smirnov test was used to assess data distribution. Continuous data normally distributed were analyzed using the Student t-test, whereas nonparametric data were

**TABLE 2. Comparison of clinical data of the two cohorts**

| Clinical Data | Pre-ERAS Cohort, n = 30 | ERAS Cohort, n = 31 | p Value |
|---|---|---|---|
| Epidemiological data | | | |
| Epidemiology | | | |
| Women | 12 (40.0%) | 23 (74.2%) | **0.0098** |
| Median age in yrs at surgery (IQR) | 54.5 (31–77.5) | 55 (18–80.5) | 0.7 |
| Comorbidities | | | |
| Hypertension | 12 (40.0%) | 12 (38.7%) | >0.99 |
| DI | 6 (20.0%) | 4 (12.9%) | 0.51 |
| Obesity | 6 (20.0%) | 11 (35.5%) | 0.25 |
| OSAS | 2 (6.7%) | 4 (12.9%) | 0.67 |
| Cardiac disease | 2 (6.7%) | 2 (6.5%) | >0.99 |
| Oncological disease | 0 (0.0%) | 0 (0.0%) | >0.99 |
| Dependencies | | | |
| Tobacco | 1 (3.3.%) | 6 (19.4%) | 0.1 |
| Alcohol | 0 (0.0%) | 1 (3.2%) | >0.99 |
| Other drugs | 0 (0.0%) | 1 (3.2%) | >0.99 |
| Surgical data | | | |
| Surgical indication | | | |
| Visual impairment | 10 (33.3%) | 7 (22.6%) | 0.4 |
| Hormonal hypersecretion | 5 (16.7%) | 9 (29.0%) | 0.36 |
| Anterior pituitary insufficiency | 4 (13.3%) | 1 (3.2%) | 0.19 |
| Apoplexy | 1 (3.3%) | 2 (6.5%) | >0.99 |
| Radiological progression | 5 (16.7%) | 6 (19.4%) | >0.99 |
| Fortuitous | 8 (26.7%) | 11 (35.5%) | 0.58 |
| Op time in mins | | | |
| Median w/ 0.05 & 0.95 %iles | 157 (106–253) | 147 (78.5–317.9) | 0.32 |
| Mean ± SD | 162.86 ± 52.42 | 159.47 ± 72.42 | |
| Intraop devices | | | |
| Compression boots | 15 (50.0%) | 31 (100.0%) | **<0.00001** |
| Intraop urinary probe | 2 (6.7%) | 1 (3.2%) | 0.61 |
| Prophylactic antibiotic therapy | | | |
| Median length in days (IQR) | 5 (4.45–7) | 1 | **<0.00001** |
| Pain management | | | |
| VAS; >4 w/in the hr after surgery | | | |
| Median (IQR) | 4.5 (0–9) | 5 (0–10) | 0.2 |
| Mean ± SD | 4.30 ± 2.68 | 5.06 ± 2.8 | |
| Morphine | | | |
| Total dose in mg (mean ± SD) | 2.38 ± 4.78 | 3.29 ± 4.04 | 0.19 |
| Length of treatment, days | 0–1 | 0–1 | >0.99 |
| PONV management | | | |
| Administration of antiemetic drugs | 8 (27.6%) | 7 (23.3%) | 0.77 |
| Antithrombotic prophylaxis | | | |
| Administration on POD1 | 9/29 (31.0%) | 22 (71.0%) | **0.002** |
| In-hospital LOS & costs | | | |
| IMCU stay in days | | | |
| Median LOS (IQR) | 1 (1–4.10) | 1 (1–3.5) | >0.99 |
| In-hospital LOS in days | | | |
| Median LOS (IQR) | 6 (5–12.1) | 5 (4–8.10) | **0.00014** |
| Rehospitalization w/in 30 days | 0 | 3/30 (10.0%) | 0.24 |

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**TABLE 2. Comparison of clinical data of the two cohorts**

| Clinical Data | Pre-ERAS Cohort, n = 30 | ERAS Cohort, n = 31 | p Value |
|---|---|---|---|
| In-hospital LOS & costs (*continued*) | | | |
| Costs in CHF | | | |
| Mean ± SD | 22,974 ± 6,644 | 21,035 ± 4,109 | 0.5 |

IQR = interquartile range; OSAS = obstructive sleep apnea syndrome; PONV = postoperative nausea and vomiting; VAS = visual analog scale.
Boldface type indicates statistical significance.

analyzed using the Mann-Whitney U-test. The Fisher exact test was used for qualitative variables. Significance was assessed at $p < 0.05$. Analyses were performed using the statistical software package Stata version 16 (StataCorp LLC) and scipy.stats, a Python library for scientific computing.

## Results

The two surgical cohorts had a similar age at surgery, but a higher prevalence of women was found in the protocol group ($p = 0.009$). Surgical indications were similar and the comorbidities of the two cohorts are summarized in Table 2. No difference was found in surgery duration. After the introduction of the protocol, we could adapt the antibiotic therapy duration according to literature evidence, and thus it became significantly shorter than before (from a median of 5 days we decreased it to 1 day; $p < 0.00001$).

Our patients did not experience any change in pain perception or in morphine use (or its derivatives) or in the administration of antiemetic drugs to prevent nausea and vomiting. Instead, we were more compliant concerning the administration of mechanical ($p < 0.00001$) and pharmacological measures to prevent DVT ($p = 0.002$).

The median LOS in the neurosurgical IMCU was sim-

**TABLE 3. Complications stratified according to Clavien-Dindo classification in the two cohorts**

| Clavien-Dindo Classification | Complications | No. of Patients, % | | p Value |
|---|---|---|---|---|
| | | Pre-ERAS, n = 30 | ERAS, n = 31 | |
| Grade I | | | | |
| | Epistaxis | 2, 6.7% | 2, 6.5% | >0.99 |
| | Urinary retention | 9, 30.0% | 8, 25.8% | 0.78 |
| Grade II | | | | |
| | Hypoglycemia | 0 | 0 | >0.99 |
| | Urinary infection | 0 | 0 | >0.99 |
| | Persistent sinusitis/rhinitis | 1/26 | 0 | 0.45 |
| | Meningitis | 0 | 1, 3.4% | >0.99 |
| | Permanent DI | 2, 6.7% | 0 | 0.24 |
| | Permanent hypocortisolism | 3, 10.3% | 1, 5.3% | 0.35 |
| | Permanent hypothyroidism | 5, 17.2% | 2, 10.5% | 0.25 |
| | DVT | 0 | 1, 3.2% | >0.99 |
| Grade III | | | | |
| Grade IIIa | | | | |
| | Surgery for abdominal hematoma | 0 | 1, 3.2% | >0.99 |
| | Lumbar drain for CSF leakage | 3, 10.0% | 0 | 0.11 |
| Grade IIIb | Surgery for CSF leakage | 1, 3.3% | 1, 3.2% | >0.99 |
| Grade IV | | | | |
| Grade IVa | | | | |
| | ICA injury | 1, 3.3% | 0 | 0.49 |
| | Pulmonary embolism | 0 | 1, 3.4% | >0.99 |
| | Pituitary apoplexy | 0 | 1, 3.2% | >0.99 |
| Grade V | | | | |
| | Death | 0 | 0 | >0.99 |

**TABLE 4. Compliance of the two cohorts with every criterion on the checklist, along with weighted average for the different phases and the total compliance**

| Criteria | Compliance of Pre-ERAS Cohort, n = 30 | Compliance of ERAS Cohort, n = 31 | p Value |
|---|---|---|---|
| Preop phase | | | |
| Anesthesiology consultation | 26 (86.7%) | 23 (74.2%) | 0.33 |
| Preop education & counseling | 0 (0%) | 20 (64.5%) | **<0.00001** |
| Endocrinological checkup | 28 (93.3%) | 31 (100%) | 0.23 |
| Ophthalmological checkup | 23 (76.7%) | 25/29 (86.2%) | 0.76 |
| CT scan of skull base | 27 (90%) | 30 (96.8%) | 0.35 |
| Pituitary MRI | 23 (76.7%) | 31 (100%) | **0.0047** |
| Endocrinology consultation the day before surgery | 22 (73.3%) | 26 (83.9%) | 0.36 |
| Preop Solu-CORTEF in the hr before surgery* | 26/29 (89.6%) | 27/28 (96.4%) | 0.61 |
| Preop avg | 73.2% | 87.7% | |
| Periop phase | | | |
| Pneumatic compression boots | 15 (50%) | 31 (100%) | **<0.00001** |
| Prophylactic antibiotic therapy | 30 (100%) | 31 (100%) | >0.99 |
| Avoidance of urinary probe during surgery | 28/30 (93.3%) | 29/30 (96.7%) | >0.99 |
| Throat packing | 9 (30%) | 31 (100%) | **<0.00001** |
| Intraop hydration <2500 ml | 29 (96.7%) | 31 (100%) | 0.49 |
| Intraop avg | 74.0% | 99.4% | |
| 24-hr postop antibiotic therapy | 2 (6.67%) | 29 (93.5%) | **<0.00001** |
| Postop Solu-CORTEF every 8 hrs for the 1st 24 hrs | 14/29 (48.3%) | 27/28 (96.4%) | **0.001** |
| Pain evaluation in the 1st hr after surgery | 13 (43.3%) | 25 (80.6%) | **0.0037** |
| Early feeding during the 4 hrs after surgery | 9 (30.0%) | 23 (74.2%) | **0.0008** |
| Postop phase | | | |
| Early mobilization w/in 6 hrs | 3/27 (11.1%) | 19 (61.3%) | **<0.00001** |
| In-hospital mobilization | Not documented | 16/30 (53.3%) | NA |
| Electrolyte controls 2×/day | 20 (66.7%) | 29 (93.5%) | 0.01 |
| Hydric balance | 28 (93.3%) | 31 (100%) | 0.24 |
| Hydrocortisone administration according to endocrinological protocol | 28 (93.3%) | 31 (100%) | 0.24 |
| Basal cortisolemia on POD3 | 25 (83.3%) | 29 (93.5%) | 0.25 |
| Discharge on POD3† | 1/9 (11.1%) | 14/14 (100%) | **<0.00001** |
| Discharge on POD5‡ | 11/21 (52.4%) | 12/17 (70.6%) | 0.33 |
| Postop avg | 52.0% | 84.5% | |
| Total weighted avg | 64.2% | 89.5% | **0.016** |

Avg = average; NA = not available.
Boldface type indicates statistical significance.
* Excluding patients with ACTH-secreting PitNET.
† After basal cortisol dosage and if the following criteria were fulfilled: patients < 75 years old and in good physical condition; no DI or controlled DI (patient's symptoms controlled with medications and normal electrolyte levels); no CSF leakage; no fever or other surgical complications; lesion was not an ACTH-secreting PitNET; and patients capable of adapting their cortisol treatment on their own (stress dosage).
‡ For all patients not fulfilling criteria for discharge on day 3 after surgery.

ilar between the two groups, but the total LOS was significantly shorter for the post-ERAS group ($p = 0.00014$). The readmission rate at 30 days after surgery was similar between the two groups.

Cost analysis showed a trend toward a less expensive in-hospital stay for the post-ERAS group (21,035 ± 4,109 Confederatio Helvetica francs [CHF]) compared to the pre-ERAS group (22,974 ± 6,644 CHF), with an average cost minimization corresponding to 1,940 CHF per stay.

Postoperative complications are detailed in Table 3. No statistically significant difference was found in complication rates between the two groups.

When considering the compliance with the checklist criteria (Table 4) since the introduction of the protocol, we found significant improvements in the education and counseling of the patients ($p < 0.00001$) as well as the performance of a dedicated pituitary MRI before surgery ($p = 0.0047$) Fig. 2. However, we were already doing well in the

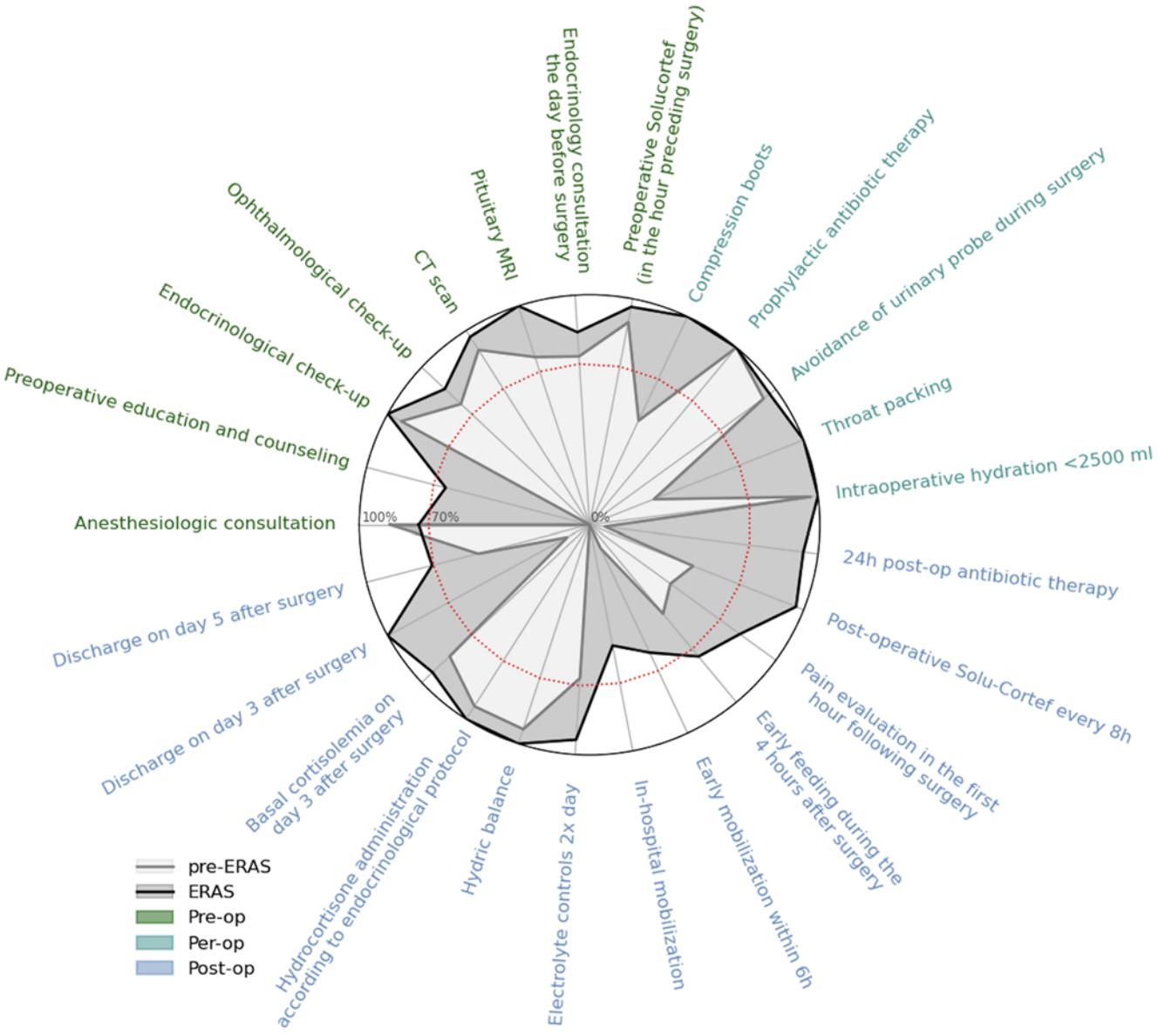


**FIG. 2.** The compliance with each criterion on the checklist is graphically represented. A compliance of at least 70% is requested for patients and medical personnel to be compliant with the ERAS protocol, and it is represented here as a *red dotted circle*. The criteria are in different colors according to the phase to which they belong. A significantly higher compliance was found in the ERAS cohort.

compliance with criteria for the preoperative phase (≥ 70%), even before the introduction of our protocol. In contrast, in the perioperative phase we significantly improved our compliance with the use of mechanical antithrombotic prevention ($p < 0.00001$) and throat packing ($p < 0.00001$). In both of these cases, a lack of documentation in the pre-ERAS group was found, thus affecting the results.

The postoperative phase was when we were able to obtain most of the improvements in the management of our patients. The duration of antibiotic therapy was adjusted to 24 hours, thereby avoiding longer therapies ($p < 0.00001$) that showed no advantages in terms of reducing infectious complications. Postoperative IV hydrocortisone (Solu-CORTEF) was administered according to a well-structured protocol every 8 hours ($p = 0.001$) in the first 24 hours after surgery; pain evaluation was systematically performed within 1 hour after the end of surgery once the protocol was introduced ($p = 0.001$); and early feeding (within 4 hours from surgery) and mobilization (within 6 hours from surgery) were more frequently performed in the ERAS cohort ($p = 0.0008$ and $p < 0.00001$, respectively).

Blood samples were also performed timely in the ERAS cohort ($p = 0.01$) and more patients were able to return home on the 3rd day after surgery in the postprotocol group ($p < 0.00001$). Details about our compliance with checklist criteria are reported in Table 4 and in Fig. 2;

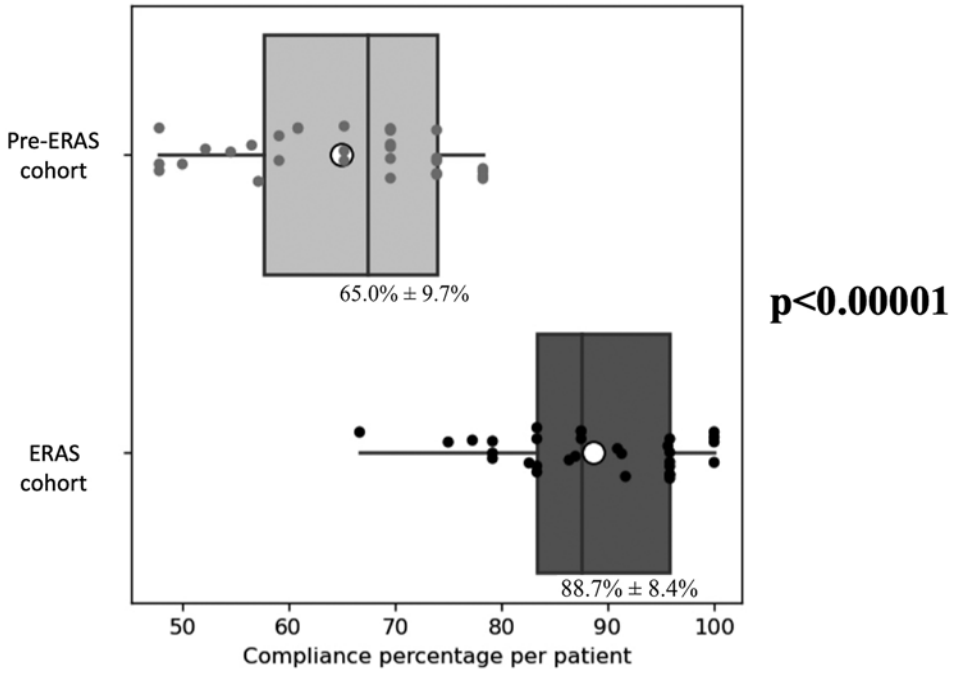


**FIG. 3.** The compliances per patient are detailed. Each *dot* represents 1 patient, and a significantly higher compliance rate was found in the ERAS cohort ($p < 0.00001$).

our compliance with the whole process significantly increased, from 64.2% to 89.5% ($p = 0.016$). The compliance per patient also significantly increased ($p < 0.00001$), as presented in Fig. 3.

## Discussion

ERAS programs use evidence-based practices to orient care pathways in multiple surgical domains,[11,20,32,39,40] and this attitude was translated into the publication of official guidelines under the aegis of the ERAS Society. Their application in neurosurgery is still in its infancy, with official guidelines recently introduced for spine surgery,[33] but none exist for cranial procedures. However, as a result of evidence from other specialties, multiple neurosurgical centers became interested in ERAS philosophy to guide patients' perioperative management. They progressively introduced local protocols for the treatment of different neurosurgical pathologies,[22,30,41] such as oncological pathologies,[24,27,42] intracranial aneurysm treatment,[25] microvascular decompression,[43] and pituitary pathologies.[23,26,28]

Implementing a multidisciplinary ERAS protocol for the management of PitNET is feasible and may bring some clear clinical, organizational, and financial advantages. The systematic delivery of ERAS programs ensures that all aspects of the perioperative care process are planned and addressed similarly in every patient.[23] Active participation by patients and caregivers is a key factor to improve compliance. The use of written protocols also facilitates understanding of the process, and the medical staff can anticipate and predict the management of other specialty team members, thus facilitating multidisciplinary collaboration. Every center presents its evidence according to its clinical practice and the supportive literature on the subject and, aside from some common items, the management has not been standardized as yet.

With our protocol we aimed to clarify the care pathway for patients with PitNET, while limiting unnecessary interventions and enhancing patient education and awareness. In our analysis, we were able to shorten the duration of antibiotic therapy without any increase in infectious complications, as supported by literature evidence.[44–46] Pain perception was similar but it was systematically assessed only after the introduction of the protocol. We also improved our adherence to prescribing mechanical and pharmacological measures to prevent DVT during and early after surgery. Concerning the surgical technique, we tried to avoid any unnecessary invasive measure. A uninostril technique was performed to respect the contralateral mucosa (except in cases of large or giant PitNET) and thus limit the risks of postoperative rhinitis and sinusitis. Furthermore, we limited the use of urinary catheters and postoperative nasal packing to allow for early mobilization and physiological nasal breathing. No nasoseptal flap or lumbar drain was used. All these results combined could explain the trend toward a reduction of the cost of the stay for the post-ERAS group. Indeed, although the difference is not statistically significant at this point, the present study confirms the cost-effectiveness of the protocol given that we improved perioperative care without increased expenses. If we consider our recruitment of 45 patients/year, a cost minimization of 1,940 CHF per stay could represent a projected annual economy of 87,300 CHF for the department.

Concerning our list of complications, major complica-

tions were found in 2 cases in the pre-ERAS era (6.7%)—namely 1 internal carotid artery (ICA) injury and 1 surgical revision for CSF leakage. ICA injury was a rare complication in our surgical series; we reported only 2 cases during the last decade, representing 0.2% of our surgical series,[47,48] a percentage that corresponds to the literature data.[49–52] Surgical revision for CSF leakage occurred in 1 patient in each cohort (3.3%), which is similar to what is reported in the literature.[53–55] Furthermore, concerning minor complications, the rates of pituitary insufficiency after surgery were similar to the literature in the field.[56–59] We had a nonnegligible rate of urinary retention after surgery, probably indicating that the hydration during surgery should be reduced to 1500 ml, except in rare cases showing early signs of intraoperative DI.

Besides the possible outcomes, a key factor to consider is the compliance with the process, which needs to be quantified. Only a compliance rate of ≥ 70% can be considered sufficient for an ERAS program. This represents an invaluable monitor of the activity of the department and it should be coupled to a continuous audit of the program, to optimize the elements belonging to the protocols and to suggest strategies to overcome barriers. If we look at the key performance indicators in our checklist, most of the improvements were made in the early postoperative management. Due to early mobilization and feeding in the hours after surgery, patients felt more comfortable in going home early. This was reflected in the total LOS, which was significantly shorter after the introduction of the protocol, and some patients could be safely discharged 3 days after surgery. No difference in the readmission rate at 30 days was found.

Larger cohorts and multicenter studies could be helpful in supporting these encouraging results as well as in standardizing the management of these patients across different countries, to ensure optimal care. We believe that the positive effects resulting from the introduction of a standardized protocol will encourage the neurosurgical community to collaborate in building international official ERAS guidelines specific for cranial neurosurgery.

## Conclusions

The certification of our neurosurgical department by the ERAS Society and the introduction of a standardized protocol for the perioperative management of patients with PitNET allowed us to achieve a multidisciplinary implementation of the management of these patients. The documentation has strongly improved since the introduction of our ERAS protocol. In this paper we propose cost-effective interventions that can improve perioperative care, offering the benefits of standardized patient management and improved data tracking. We were able to reduce invasive measures and unnecessary treatments while achieving significant improvements in terms of early mobilization and feeding, thereby resulting in a shorter hospital stay.

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## Disclosures

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

## Author Contributions

Conception and design: Messerer, Cossu, Belouaer, Gaudet, Papadakis. Acquisition of data: Messerer, Cossu, Belouaer, Caliman, Agri, Gaudet. Analysis and interpretation of data: Messerer, Cossu, Belouaer, Kloeckner, Caliman, Agri, Daniel, Papadakis. Drafting the article: Messerer, Cossu, Belouaer, Daniel, Gaudet. Critically revising the article: Messerer, Cossu, Belouaer, Kloeckner, Caliman, Agri, Gaudet. Reviewed submitted version of manuscript: Messerer, Cossu, Belouaer, Kloeckner, Agri, Papadakis. Approved the final version of the manuscript on behalf of all authors: Messerer. Statistical analysis: Messerer, Cossu, Belouaer, Kloeckner, Agri. Administrative/technical/material support: Belouaer. Study supervision: Messerer, Daniel.

## Supplemental Information

### Online-Only Content

Supplemental material is available online.

*Supplemental Figs. 1–3*. https://thejns.org/doi/suppl/10.3171/2023.9.FOCUS23529.

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