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# Incidence and Risk Factors for Prolonged Hospitalization and Readmission after Transsphenoidal Pituitary Surgery

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## Abstract

*Objective*. To evaluate the incidence and factors associated with 30-day readmission and to analyze risk factors for prolonged hospital length of stay following transsphenoidal pituitary surgery.

*Study Design*. Retrospective longitudinal claims analysis.

*Setting*. American College of Surgeons National Surgical Quality Improvement Program.

*Subjects and Methods*. The database of the American College of Surgeons National Surgical Quality Improvement Program was queried for patients who underwent transsphenoidal pituitary surgery (*Current Procedural Terminology* code 61548 or 62165) between 2005 and 2014. Patient demographic information, indications for surgery, and incidence of hospital readmission and length of stay were reviewed. Risk factors for readmission and prolonged length of stay, defined as >75th percentile for the cohort, were identified through logistic regression modeling.

*Results*. A total of 1006 patients were included for analysis. Mean hospital length of stay after surgery was 4.1 ± 0.2 days. Predictors of prolonged length of stay were operative time ($P < .001$, odds ratio [OR] = 1.7, 95% confidence interval [95% CI] = 1.5-2.0), bleeding disorder ($P = .049$, OR = 3.1, 95% CI = 1.0-9.5), insulin-dependent diabetes ($P = .007$, OR = 2.4, 95% CI = 1.3-4.4), and reoperation ($P < .001$, OR = 10.3, 95% CI = 4.7-23.9). In a subset analysis of 529 patients who had surgery between 2012 and 2014, 7.2% (n = 38) required hospital readmission. History of congestive heart failure (CHF) was a predictor of hospital readmission ($P = 0.03$, OR = 12.7, 95% CI = 1.1-144.0).

*Conclusion*. This review of a large validated surgical database demonstrates that CHF is an independent predictor of hospital readmission after transsphenoidal surgery. Although CHF is a known risk factor for postoperative complications, it poses unique challenges to patients with potential postoperative pituitary dysfunction.

## Keywords

transsphenoidal, pituitary surgery, readmission, length of stay, National Surgical Quality Improvement Program

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Hospital readmission after surgery adversely affects patient quality of life and has become an important health care quality indicator used by Centers for Medicare and Medicaid Services to determine hospital reimbursement.[1] With the institution of the Affordable Care Act and its associated Hospital Readmissions Reduction Program (HRRP), efforts have increased to identify risk factors for 30-day hospital readmission among surgical patients. In 2004, 15.6% of all surgical Medicare patients were readmitted to the hospital within 30 days of discharge, and overall Medicare expenditures for unplanned readmissions totaled $17.4 billion.[2] Beginning in 2012, HRRP required Centers for Medicare and Medicaid Services to reduce payments to hospitals with excess readmissions.[3] While otolaryngologic operations are not yet among those directly targeted by HRRP, future expansion of its scope of procedures and diagnoses is likely to affect our specialty.

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Prior studies in the literature have indicated that, while uncommon, readmission following pituitary surgery is costly. In a review of 30-day readmissions among 466 patients who underwent endoscopic transsphenoidal pituitary surgery, Hendricks et al found an overall readmission rate of 6.2% at an average cost of $10,760 per readmission. Among patients who were readmitted for cerebrospinal fluid (CSF) leak, readmission reached an average cost of $24,613 per readmission. The most frequent causes of readmission were epistaxis (2.1%), hyponatremia (1.5%), and CSF leak (0.9%).[4] In a series of 303 patients who underwent transsphenoidal surgery, Bohl et al found an overall readmission rate of 8.9%, with the most frequent reasons for readmission being hyponatremia (5.0%), diabetes insipidus (1.3%) and adrenal insufficiency (0.7%).[5] As expected, the major causes of readmission after transsphenoidal surgery were related to postoperative complications (eg, epistaxis, CSF leak) and endocrine dysfunction.

Further understanding is needed of the risk factors that predispose patients to prolonged hospital stay and readmission after transsphenoidal pituitary surgery. Through identification of these factors, strategies and risk-reductive interventions can be implemented to mitigate these costly occurrences. The objective of this study was to evaluate the incidence, causes, and risk factors for 30-day readmission and increased hospital length of stay following transsphenoidal pituitary surgery using the American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP).

## Materials and Methods

The 2005-2014 ACS NSQIP databases were reviewed to identify encounters for which transsphenoidal approach to resection of the pituitary was performed. Reviewed cases were those that included either of the following 2012 *Current Procedural Terminology* codes: 62165 or 61548. Only cases listed as being admitted from home were included. Patients who underwent concurrent craniotomy were identified by *Current Procedural Terminology* code and excluded to avoid including patients who underwent transcranial or combined approaches to the pituitary. This study was determined to be exempt by the Institutional Review Board of the Hospital of the University of Pennsylvania.

Patient encounters were identified within the participant use data files of the ACS NSQIP, which in 2014 included 517 community and academic hospitals throughout the United States with 323 variables for each case.[6] Data are collected by trained nurses at participating institutions through systematic sampling of major operations performed. Each variable in the database is specifically defined, and data collectors are periodically audited to ensure standardization and accuracy of the content. To ensure a 30-day follow-up period, patients are contacted by letter or telephone survey following discharge. The list and definitions of variables collected in the database can be found at the ACS NSQIP website (https://www.facs.org/quality-programs/acs-nsqip). In addition to the predefined ACS NSQIP variables, we calculated body mass index (BMI; in $kg/m^2$) for each encounter. Operative time was converted to hours for analysis.

Additional reoperation and readmission information is available for cases that were performed in or after 2012, and readmission analysis was performed on this subset of data. Specifically, the reasons for hospital readmission, including readmission-related *ICD-9* codes (*International Classification of Diseases, Ninth Revision*) were collected in the ACS NSQIP database beginning in 2012. Previous studies seeking to assess the validity of the ACS NSQIP readmissions data have shown good agreement with institutional medical records and administrative data.[7]

The primary outcomes of interest were hospital length of stay and readmission within 30 days of the primary procedure. Logistic regression was performed to determine factors affecting the primary outcome measures. A prolonged length of stay was defined as postoperative hospital stay >75th percentile for the entire cohort.[8] To obtain the variables included in the final model, univariate comparison of all input variables was performed with Pearson $\chi^2$ for categorical variables or Mann-Whitney tests for continuous variables. Those variables with $P < .2$ on univariate analysis and <10% missing data were included in the preliminary logistic model. Only cases with complete data for the variables of interest were included in the model. A forward and backward stepwise regression algorithm was then used to select the best model by minimizing the Akaike information criterion to determine the final model. Variables with $P < .05$ on the final multivariate logistic model were considered significant. Linear regression for length of stay in days was performed in a similar manner. All data processing and analysis were performed with R version 3.2.1 (https://www.r-project.org) via RStudio version 0.99.467 (RStudio, Boston, Massachusetts).

## Results

A total of 1006 transsphenoidal operations were included in the ACS NSQIP database between 2005 and 2014 as defined above. Patient demographic information is shown in **Table 1**. The most common indication for transsphenoidal surgery was benign pituitary neoplasm (*ICD-9* 227.3), which accounted for 79.6% of cases (see **Table 2**). Transsphenoidal surgery was performed for malignancy in approximately 1% of cases. Mean operative time was 2 hours 32 minutes ± 2.6 minutes. There were 6 postoperative deaths within 30 days of the primary procedure (0.6%), which occurred at a mean of postoperative day 8.8 ± 0.3.

### *Hospital Length of Stay*

Mean hospital length of stay after transsphenoidal pituitary surgery was 4.1 ± 0.2 days. Risk factors for prolonged length of stay on multivariate logistic regression include operative time (hours; $P < .001$, odds ratio [OR] = 1.72, 95% confidence interval [95% CI] = 1.5-2.0), bleeding disorder ($P = .049$, OR = 3.1, 95% CI = 1.0-9.5), insulin-dependent diabetes ($P = .007$, OR = 2.4, 95% CI = 1.3-4.4),

**Table 1.** Demographic Information for Subjects Meeting Inclusion Criteria.

| Variable | n (%) or Mean ± SD |
|---|---|
| Sex | |
| Female | 524 (52.1) |
| Male | 480 (47.7) |
| Race | |
| Black or African American | 141 (14.0) |
| Other | 79 (7.9) |
| White | 643 (63.9) |
| Unknown/not reported | 111 (11.0) |
| Age, y | 54.0 ± 0.5 |
| Body mass index, kg/m$^2$ | 31.3 ± 0.2 |

white blood cell count ($P$ = .03, OR = 1.1, 95% CI = 1.0-1.1), and reoperation ($P < .001$, OR = 10.3, 95% CI = 4.7-23.9). Increasing preoperative hematocrit was found to be protective ($P$ = .003, OR = 0.94, 95% CI = 0.9-0.98). See **Table 3** and **Figure 1**.

Linear regression was also performed, which revealed that operative time (hours; $P < .001$, slope = 1.01), emergency case ($P$ = .008, slope = 4.5), partially dependent functional status ($P < .001$, slope = 5.6), and return to the operating room ($P < .001$, slope = 7.5) significantly affected the length of stay.

### *Hospital Readmission*

Of 529 patients who had surgery in or after 2012, 38 (7.2%) required hospital readmission at a mean of 13.7 ± 0.3 days after surgery. The most common indications for hospital readmission are shown in **Table 4**. History of congestive heart failure (CHF) was highly associated with readmission on multivariate analysis ($P$ = .03, OR = 12.7, 95% CI = 1.1, 143; see **Table 5** and **Figure 2**). In the same subset of patients who had surgery in 2012 or later, 28 patients (5.3%) required reoperation related to the original surgery at a mean of postoperative day 10.8 ± 0.4. Of these, 11 patients (39.3%) underwent reoperation during the initial hospitalization, and 17 (60.7%) required reoperation following hospital readmission. Twelve patients (2.3%) underwent operative intervention for the management of a postoperative CSF leak.

## Discussion

Transsphenoidal pituitary surgery is a safe and effective surgical approach for treating pituitary tumors and carries <1% risk of mortality.[9] With advances in technology, endoscopic endonasal techniques have increased in popularity over traditional microscopic techniques for resection of pituitary tumors.[10] The literature shows that, while rare, readmission after transsphenoidal surgery is associated with significant added cost. Recent health care reform has identified unplanned hospital readmission as a large source of preventable health care spending in the United States. In this study, we studied reasons for hospital readmission and identified several independently associated perioperative factors associated with increased length of hospital stay and readmission in patients who underwent transsphenoidal surgery.

Overall, 7.2% of patients who underwent transsphenoidal pituitary surgery in the ACS NSQIP database in 2012 or later were readmitted to the hospital within 30 days of surgery. The most common reasons for readmission were similar to those identified in prior studies and included endocrine dysfunction (eg, hyponatremia) and postoperative complications (eg, epistaxis, CSF leak).[11] History of CHF was the only statistically significant risk factor for hospital readmission identified on multivariate analysis.

This is the first study to identify a link between CHF and hospital readmission after transsphenoidal surgery and may be the basis for future studies evaluating unique perioperative care pathways for patients with CHF to reduce readmission after transsphenoidal surgery. There already exists an expansive body of literature studying risk factors for hospital readmission among patients with CHF. Among these, hyponatremia is widely accepted to be associated with increased morbidity and mortality among patients with CHF.[12,13] While it is unknown why patients with CHF are at increased risk of hospital readmission after transsphenoidal surgery, it is likely that heart failure,

**Table 2.** Most Common Indications by *ICD-9* Code for Patients Who Underwent Transsphenoidal Pituitary Surgery in the ACS NSQIP.

| *ICD-9* | Description | n (%) |
|---|---|---|
| 227.3 | Benign neoplasm of pituitary gland and craniopharyngeal duct | 801 (79.6) |
| 253.8 | Other disorders of the pituitary and other syndromes of diencephalohypophysial origin | 38 (3.8) |
| 237.0 | Neoplasm of unspecified nature of endocrine glands and other parts of nervous system | 34 (3.4) |
| 239.7 | Neoplasm of uncertain behavior of pituitary gland and craniopharyngeal duct | 30 (3.0) |
| 253.9 | Cushing's syndrome | 11 (1.1) |
| 255.0 | Malignant neoplasm of pituitary gland and craniopharyngeal duct | 10 (1.1) |
| 194.3 | Benign neoplasm of cranial nerves | 8 (0.8) |
| 225.1 | Unspecified disorder of the pituitary gland and its hypothalamic control | 6 (0.6) |

Abbreviations: ACS NSQIP, American College of Surgeons National Surgical Quality Improvement Program; *ICD-9, International Classification of Diseases, Ninth Revision*.

**Table 3.** Risk Factors Predictive of Prolonged Hospital Length of Stay after Transsphenoidal Pituitary Surgery on Multivariate Analysis.

| Risk Factor | *P* Value | Odds Ratio | SEM | 95% CI |
|---|---|---|---|---|
| Reoperation | <.001 | 10.3 | 0.4 | 4.7-23.9 |
| Contaminated wound | .06 | — | — | — |
| Bleeding disorder | .049 | 3.1 | 0.6 | 1.0-9.5 |
| IDDM | .007 | 2.4 | 0.3 | 1.3-4.4 |
| Operative time, h | <.001 | 1.7 | 0.07 | 1.5-2.0 |
| Preoperative WBC | .03 | 1.06 | 0.03 | 1.0-1.1 |
| Preoperative HCT | .004 | 0.94 | 0.02 | 0.9-1.0 |
| Non-IDDM | .70 | — | — | — |
| Clean-contaminated wound | .21 | — | — | — |
| Male sex | .12 | — | — | — |
| Dyspnea with moderate exertion | .39 | — | — | — |
| Dirty/infected wound | .37 | — | — | — |

Abbreviations: 95% CI, 95% confidence interval; HCT, hematocrit; IDDM-insulin-dependent diabetes mellitus; SEM, standard error of the mean; WBC, white blood cell count.

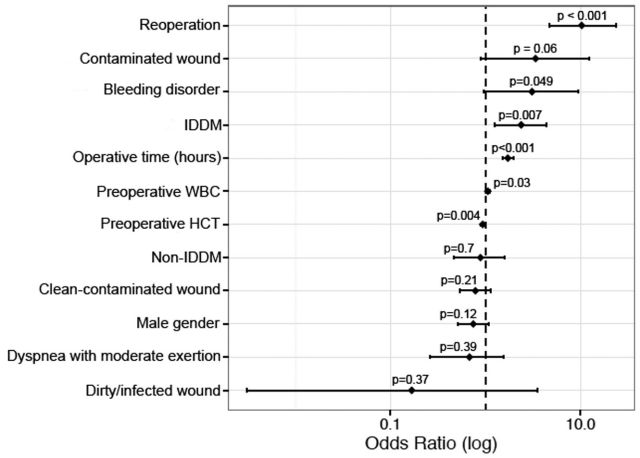


**Figure 1.** Forest plot of risk factors for prolonged hospital length of stay. Odds ratio with 95% confidence interval and *P* value shown for each variable. HCT, hematocrit; IDDM, insulin-dependent diabetes mellitus; WBC, white blood cell count.

**Table 4.** Causes of Hospital Readmission among Patients Who Underwent Transsphenoidal Pituitary Surgery between 2012 and 2014.

| Cause of Readmission | n (%) |
|---|---|
| Cerebrospinal fluid rhinorrhea | 8 (1.5) |
| Delayed hyponatremia | 7 (1.3) |
| Epistaxis | 3 (0.6) |
| Stroke | 1 (0.2) |
| Pulmonary embolism | 1 (0.2) |
| Sepsis | 1 (0.2) |
| Wound disruption | 1 (0.2) |
| Iatrogenic hypopituitarism | 1 (0.2) |
| Migraine | 1 (0.2) |
| Fever | 1 (0.2) |
| Nausea and vomiting | 1 (0.2) |
| Fall | 1 (0.2) |
| Other/unknown | 11 (2.1) |
| Total | 38 (7.2) |

when combined with pituitary surgery, may increase the risk of electrolyte abnormalities that lead to hospital readmission in the postoperative period. This and prior studies have shown hyponatremia to be a leading cause of hospital readmission after pituitary surgery.[4,5] CHF frequently manifests as hypervolemic hyponatremia, which occurs when body sodium and water are both in excess but the increase in total body water exceeds the total body sodium level, resulting in edema.[12] Furthermore, when postoperative hyponatremia occurs due to pituitary dysfunction, it may exacerbate heart failure and lead to hospital readmission. Unfortunately, due to the limitations of large data sets, we were unable to definitively determine the electrolyte status of all readmissions. Further studies are needed to clarify the association between history of CHF and hospital readmission after transsphenoidal pituitary surgery.

The mean length of stay of 4.1 ± 0.2 days in the ACS NSQIP series is similar to that found by prior studies.[5,9] Length of stay ranged from 0 to 111 days, and median hospital length of stay was 3 days. For this analysis, we defined prolonged length of stay as any within the upper quartile of cases in this series (>4 days). Due to positive skew caused by a small number of cases with very long lengths of stay, the mean and 75th percentile values were similar. However, this had no significant effect on subsequent data analysis. Our results showed that factors associated with prolonged hospital length of stay included operative time, lower preoperative hematocrit, higher preoperative white blood cell count, insulin-dependent diabetes, and history of bleeding disorder (see **Figures 1** and **2**). While statistically significant on multivariate analysis, the odds ratios associated with preoperative hematocrit and white blood cell (0.94 and 1.06, respectively) were approximately 1, indicating that these

**Table 5.** Risk Factors Predictive of Hospital Readmission after Transsphenoidal Pituitary Surgery on Multivariate Analysis.

| Risk Factor | *P* Value | Odds Ratio | SEM | 95% CI |
|---|---|---|---|---|
| History of CHF | .03 | 12.7 | 1.2 | 1.1-144 |
| Bleeding disorder | .1 | — | — | — |
| Chronic steroid use | .1 | — | — | — |
| IDDM | .2 | — | — | — |
| Non-IDDM | .2 | — | — | — |

Abbreviations: 95% CI, 95% confidence interval; CHF, congestive heart failure; IDDM, insulin-dependent diabetes mellitus; SEM, standard error of the mean.

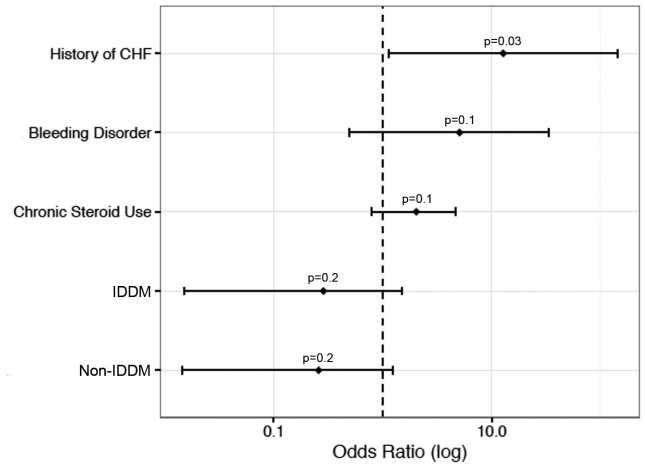


**Figure 2.** Forest plot of risk factors for hospital readmission. Odds ratio with 95% confidence interval and *P* value shown for each variable. CHF, congestive heart failure; IDDM, insulin-dependent diabetes mellitus.

factors had relatively little impact on hospital length of stay and were likely not clinically meaningful. Operative time predicted prolonged length of stay with an increase in odds of approximately 72% with each additional hour. Prior studies have shown time under general anesthesia to be associated with postoperative complications and hospital length of stay in patients undergoing head and neck surgery.[14] Similarly, diabetes mellitus has been shown to be a risk factor for perioperative complications after transsphenoidal surgery.[15] The association between diabetes and increased hospital length of stay is likely related to an increased risk of perioperative complications in the diabetic population and has been described in the cervical spine surgery literature.[16] Finally, history of bleeding disorder—including preoperative anticoagulation that was continued to the time of surgery—was predictive of greater-than-average length of stay with an odds ratio of 3.1, likely due to increased risk of epistaxis. Linear regression analysis demonstrated that each additional hour in the operating room, emergency surgery, a partially dependent functional status, and return to the operating room extended length of stay by an average of 1, 4, 6, and 8 days, respectively.

Overall, reoperation occurred in 5.3% of cases and was most commonly performed to repair a delayed CSF leak. This finding is consistent with our own institution's experience and the existing literature relating to reoperation after transsphenoidal surgery.[4,17] For the purposes of identifying risk factors for prolonged length of stay and readmission, only reoperations that occurred during the initial hospitalization (11 cases) were included for analysis. Reoperation was significantly associated with prolonged length of stay ($P < .001$, OR = 10.3, 95% CI = 4.7-23.9) but not readmission ($P = .69$).

A recently published study of predictors of 30-day morbidity and mortality after pituitary surgery, based on 658 patients in the ACS NSQIP database, also included an analysis of predictors of increased length of hospital stay. The authors reported that older age, higher BMI, chronic steroid use, preoperative sepsis, and lower preoperative serum albumin were associated with increased length of hospital stay.[18] However, similar analysis of the effects of preoperative serum albumin was not possible in our cohort given the large number of missing values in the ACS NSQIP. With the inclusion of 365 additional cases from 2013 and 2014, age, BMI, chronic steroid use, and sepsis were not found to be significant predictors of increased length of stay.

Unfortunately, significant limitations exist in this analysis of risk factors for prolonged hospital length of stay and readmission after transsphenoidal pituitary surgery, based on a large, risk-adjusted national database. First, the ACS NSQIP is designed to track a variety of operations and therefore includes numerous variables. Unfortunately, several procedure-specific complications or variables associated with pituitary surgery are not currently included. For example, the incidence of intra- or postoperative CSF leak is impossible to discern in the ACS NSQIP because there is no specific field to capture these events. Furthermore, data regarding tumor factors, including size, location, suprasellar extension, and postoperative endocrine dysfunction, are not available. As with all large databases, missing data pose a significant challenge in the ACS NSQIP and is a significant limitation of this study. Of 38 patients who were readmitted to the hospital, the reason for readmission was either absent or unable to be discerned from the available data of 11 patients (28.9%). While numerous statistical approaches are employed to limit the effects of missing data in the ACS NSQIP, these methods are imperfect, and missing data remain a significant limitation of large database studies.[19] Another limitation of this analysis is the lack of data to

determine how many patients underwent transsphenoidal pituitary surgery via an endonasal endoscopic or microscopic approach. However, this is likely not a major limitation, as previous studies have failed to show significant differences in postoperative outcomes between the endoscopic and microscopic techniques.[20,21]

## Conclusions

Prolonged hospital length of stay and readmission after transsphenoidal pituitary surgery are a substantial cause of preventable health care expenditure. We have presented a series of 1006 cases from the ACS NSQIP database and demonstrated that operative time, insulin-dependent diabetes, and history of a bleeding disorder are risk factors for prolonged length of stay. Additionally, a history of CHF is an independent risk factor for hospital readmission after transsphenoidal pituitary surgery on multivariate analysis. This is likely due to a greater sensitivity to electrolyte disturbance in this patient population. We believe that these findings will be useful to clinicians in improving preoperative optimization and developing postoperative protocols designed to reduce hospital length of stay and minimize unplanned readmission after transsphenoidal pituitary surgery.

### Author Contributions

**Andrés M. Bur**, study design and conception, data analysis and interpretation, literature review, manuscript draft, revision, and final approval; **Jason A. Brant**, study design and conception, data analysis and interpretation, manuscript draft, revision, and final approval; **Jason G. Newman**, data interpretation, manuscript revision, and final approval; **Kyle M. Hatten**, data interpretation, manuscript revision, and final approval; **Steven B. Cannady**, data interpretation, manuscript revision, and final approval; **John P. Fischer**, study design, data interpretation, manuscript revision, and final approval; **John Y. K. Lee**, data interpretation, manuscript revision, and final approval; **Nithin D. Adappa**, study design and conception, data interpretation, manuscript revision, and final approval.

### Disclosures

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