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# Differences in Outcomes Based on Sex for Pediatric Patients Undergoing Pyloromyotomy

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## Abstract

**Background:** Males and females are known to have varied responses to medical interventions. Our study aimed to determine the effect of sex on surgical outcomes after pyloromyotomy.

**Materials and methods:** Using the Kids' Inpatient Database for the years 2003–2012, we performed a serial, cross-sectional analysis of a nationally representative sample of all patients aged <1 y who underwent pyloromyotomy for hypertrophic pyloric stenosis. The primary predictor of interest was sex. Outcomes included mortality, in-hospital complications, cost, and length of stay. Regression models were adjusted by race, age group, comorbidity, complications, and whether operation was performed on the day of admission with region and year fixed effects.

**Results:** Of 48,834 weighted operations, 81.8% were in males and 18.2% were in females. The most common reported race was white (47.3%) and most of the patients were ≥29 days old (72.5%). There was no difference in the odds of postoperative complications, but females had a significantly longer length of stay (incidence rate ratio, 1.28; 95% confidence interval [95% CI], 1.18–1.39; $P \leq 0.01$), higher cost (5%, 95% CI, 1.02–1.08; $P \leq 0.01$), and higher odds of mortality (odds ratio, 3.26; 95% CI, 1.52–6.98; $P \leq 0.01$).

**Conclusions:** Our study demonstrated that females had worse outcomes after pyloromyotomy compared with males. These findings are striking and are important to consider when treating either sex to help set physician and family expectations perioperatively. Further studies are needed

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to determine why such differences exist and to develop targeted treatment strategies for both females and males with pyloric stenosis.

### Keywords

Gender; Sex differences; Pyloromyotomy; Male; Female

## Introduction

There has been increasing attention paid to gender-specific differences in patient care and postoperative outcomes. For instance, previous data have shown differences between genders with severity of Crohn's disease,[1] postoperative course after coronary artery bypass grafting (CABG) operations,[2] hospital course after trauma,[3–6] and outcomes after cholecystectomy operations.[7–10] Despite the budding interest in this topic, gender differences in outcomes after pediatric operations are not yet well studied. Because we know that males have a predisposition for hypertrophic pyloric stenosis (HPS),[11,12] we elected to study gender differences after pyloromyotomy, a common pediatric surgical operation. We hypothesized that there would be a difference between males and females in postoperative outcomes after pyloromyotomy.

## Materials and methods

### Data source

The Kids' Inpatient Database (KID) from the Healthcare Cost and Utilization Project was used for the analyses. The KID comprises pediatric inpatient discharge data from participating nonfederal hospitals, including general, specialty, public, and academic medical centers.[13] The data are released every 3 y, are a weighted sample of hospital discharges, and include patients from the United States who are younger than 21 y. KID reports on basic hospital characteristics, children's hospital designation, teaching hospital status, demographics, insurance status, diagnoses, performed procedures, hospital length of stay (LOS), and charges. This study was exempted from Institutional Review Board approval by the Human Subjects Committee at Harbor-UCLA Medical Center.

### Study population

We performed a review of all children younger than 1 y who underwent a pyloromyotomy for HPS during the years 2003, 2006, 2009, and 2012. To capture patients with this diagnosis, we searched using the International Classification of Diseases, Ninth Revision (ICD-9) procedure codes 43.3 (pyloromyotomy) and 44.2 (pyloroplasty) with diagnosis code 750.5 (congenital HPS).

### Measurement

The primary predictor of interest was sex, that is, male *versus* female. We evaluated rates of mortality, rates of any complication during the patient's hospitalization (during procedure, gastrointestinal, respiratory, and cardiovascular), hospital cost (calculated using cost to charge ratios[14] and published medical consumer price index), and LOS. Complications noted previously were those that are commonly seen during pyloromyotomy and we determined their rates using ICD-9 codes (Table 1).

### Statistical analysis

All regression models were adjusted for race, age group, and whether the surgeries were performed on the day of admission with region and year fixed effects. Mortality, cost, and LOS were additionally adjusted for the occurrence of any complication. Both bivariate and multivariable analyses were performed to compare males and female outcomes after pyloromyotomy. We performed logistic regression for complication and mortality rates, negative binomial regression for LOS, and multivariable linear regression for cost analysis. The cost is presented as a log-transformed value to normalize the data and adjusted to 2010 U.S. dollars.[15,16] All analyses included discharge weights provided in the KID to calculate population estimates. Comorbidities that we included were history of prematurity, pulmonary disease, or cardiovascular diseases (Table 1). All analyses used STATA version 14.2 (College Station, TX) with the SVY function to obtain nationally representative estimates weighted by the Agency for Healthcare Research and Quality-specified discharge values in compliance with Healthcare Cost and Utilization Project analysis recommendations. A $P$-value < 0.05 was considered significant and was generated from weighted regression models.

## Results

There were a total of 48,834 weighted operations reviewed between 2003 and 2012, with most patients being male (81.8% male *versus* 18.2% female). Demographic information is described in Table 2. Males were more likely to be white, and females were more likely to be from the south. Age for infants younger than 1 y is reported by the KID as either more than or less than 29 days of age, and we noted that females were more likely to be older than 29 days of age than males (83.4% females *versus* 79.5% males, $P < 0.01$). On univariate analysis (Table 3), it was noted that girls had higher postoperative mortality (0.05% male *versus* 0.30% female, $P < 0.01$) and morbidity (1.50% male *versus* 1.90% female, $P < 0.02$). Female patients were also associated with an increased average cost per hospital stay (geometric mean of $5075 male *versus* $5540 female, $P < 0.01$) and a longer LOS (geometric mean of 2.33 male *versus* 2.70 female, $P < 0.01$). Multivariable analysis (Table 4) showed that being a female was statistically significantly associated with a higher mortality rate, higher cost, and longer LOS. We estimated that, on average, females had an approximately 3 times odds of mortality (odds ratio [OR] 3.26, 95% confidence interval [CI]: 1.52–6.98, $P < 0.01$), a 5% higher cost (1.05, 95% CI: 1.02–1.08, $P < 0.01$), and a 28% longer LOS (incidence rate ratio [IRR] 1.28, 95% CI: 1.18–1.39, $P < 0.01$).

## Discussion

Our study continues to support that males and females may have different postoperative outcomes. As expected, most of the patients with pyloric stenosis were males. Nonetheless, we found that females were associated with a higher rate of mortality, a higher cost, and a longer LOS. Although the rates of mortality and morbidity were generally low for both genders, the differences between males and females were still noteworthy.

Despite the recent attention paid to the varied responses of genders to medical interventions, data on pediatric surgical patients are extremely limited and very few studies have discussed any differences specifically related to pyloric stenosis.[17,18] Literature at this time is primarily focused on the adult population and differences in response to medications. In the surgical literature, some examples of gender differences that have been described include the severity of Crohn's disease,[1] outcomes after CABG operations,[2] trauma,[3–6] and cholecystectomies.[7–10] For Crohn's disease, females have been associated with increased severity, but males with higher likelihood of growth failure.[1] After CABG operations, females have been noted to have a more lengthy and complicated course of recovery.[2] Several studies have examined outcomes after trauma, and the general consensus was that males had higher rates of mortality and morbidity, as well as longer intensive care unit stays and LOS.[3–6] Data published on outcomes after cholecystectomy have noted that males have an increased rate of conversion to open cholecystectomy,[7,8] increased rates of gangrenous cholecystitis,[9] and a generally increased postoperative morbidity.[10] These findings were attributed in large part to higher rates of medical comorbidities in males and a later presentation. In regard to increased average hospital cost and LOS, previous studies have associated females with increased health care utilization,[19,20] but these studies concentrate on general medical utilization, and data focusing specifically on utilization after pediatric operations are lacking.

The reasons behind these gender differences have not yet been well elucidated. Studies in the trauma literature suggest that males may have worse outcomes in the post-traumatic inflammatory state as their hormonal variations may predispose them to certain responses of the immune system that lead to increased susceptibility to organ damage.[21–24] As both trauma and surgery can cause a proinflammatory state, our findings of females having worse outcomes was contradictory to this theory. Another possible explanation for this disparity is differences in presentation leading to delays in diagnosis. As pyloric stenosis is far less common in females, suspicion is often low and females may present later and with more metabolic derangements,[17] predisposing them to worse outcomes. However, it is assumed that during preoperative resuscitation, metabolic derangements for both genders are corrected to a baseline level, which should correct for any discrepancy in their presenting states. Females and males have also been known to respond to medications,[25] such as antibiotics, differently, which could account for their varied rates of morbidity.

Our study is limited by the retrospective design using a large database with a potentially biased inpatient-only sample and potential coding issues. A specific limitation of obtaining data via ICD-9 coding is the inability to discern different operative techniques or rates of reoperation. We were also unable to access details such as operating surgeon specialty or laboratory or imaging results. The KID is also only reported every third year, and data were only available up until 2012 at the time of this study. Our study is novel as gender differences in postoperative outcomes in the pediatric surgery population have not yet been well studied. Future directions include measuring the impact that the increased LOS had in terms of any nosocomial complications or increased cost.

## Conclusions

In conclusion, although pyloric stenosis is more common in males, females have worse postoperative outcomes after pyloromyotomy. Females were associated with higher rates of mortality, hospital cost, and LOS. This information is vital to anticipate preoperatively and to help set patient and family expectations. The cause of this discrepancy will need to be determined in subsequent studies to enable prevention in the future.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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## REFERENCES

1. Gupta N, Bostrom AG, Kirschner BS, et al. Gender differences in presentation and course of disease in pediatric patients with Crohn disease. Pediatrics. 2007;120:e1418–e1425. [PubMed: 18055660]
2. Vaccarino V, Lin ZQ, Kasl SV, et al. Gender differences in recovery after coronary artery bypass surgery. J Am Coll Cardiol. 2003;41:307–314. [PubMed: 12535827]
3. Napolitano LM, Greco ME, Rodriguez A, et al. Gender differences in adverse outcomes after blunt trauma. J Trauma. 2001;50:274–280. [PubMed: 11242292]
4. Roof RL, Hall ED. Gender differences in acute CNS trauma and stroke: neuroprotective effects of estrogen and progesterone. J Neurotrauma. 2000;17:367–388. [PubMed: 10833057]
5. Jeschke MG, Barrow RE, Micak RP, et al. Endogenous anabolic hormones and hypermetabolism: effect of trauma and gender differences. Ann Surg. 2005;241:759–767. [PubMed: 15849511]
6. Mostafa G, Huynh T, Sing RF, et al. Gender-related outcomes in trauma. J Trauma. 2002;53:430–434. [PubMed: 12352476]
7. Zisman A, Gold-Deutch R, Zisman E, et al. Is male gender a risk factor for conversion of laparoscopic into open cholecystectomy? Surg Endosc. 1996;10:892–894. [PubMed: 8703145]
8. Genc V, Sulaimanov M, Cipe G, et al. What necessitates the conversion to open cholecystectomy? A retrospective analysis of 5164 consecutive laparoscopic operations. Clinics (Sao Paolo). 2011;66:417–420.
9. Merriam LT, Kanaan SA, Dawes LG, et al. Gangrenous cholecystitis: analysis of risk factors and experience with laparoscopic cholecystectomy. Surgery. 1999;126:680–685. [PubMed: 10520915]
10. Botaitis S, Polychronidis A, Pitiakoudis M, et al. Does gender affect laparoscopic cholecystectomy? Surg Laparosc Endosc Percutan Tech. 2008;18:157–161. [PubMed: 18427334]
11. Gibbs MK, Van Herrden JA, Lynn HB. Congenital hypertrophic pyloric stenosis. Surgical experience. Mayo Clin Proc. 1975;50:312–316. [PubMed: 1127996]
12. Spicer RD. Infantile hypertrophic pyloric stenosis: a review. Br J Surg. 1982;69:128–135. [PubMed: 7039756]
13. HCUP Kids' Inpatient Database (KID): Healthcare Cost and Utilization Project (HCUP). 1997, 2000, 2003, 2006, 2009, and 2012. Agency for Healthcare Research and Quality, Rockville, MD. www.hcup-us.ahrq.gov/kidoverview.jsp. Accessed August 8, 2019.

14. Healthcare Costs and Utilization Project - Cost-to-Charge Ratio Files: Agency for Healthcare Research and Quality, Rockville, MD. www.hcup-us.ahrq.gov/db/state/costtocharge.jsp. Accessed August 8, 2019.

15. Hasegawa K, Tsugawa Y, Brown DFM, Camargo CA. Childhood asthma hospitalizations in the United States, 2000–2009. J Pediatr. 2013;163:1127–1133. [PubMed: 23769497]

16. Hasegawa K, Tsugawa Y, Brown DFM, Mansbach JM, Camargo CA. Trends in bronchiolitis hospitalizations in the United States, 2000–2009. Pediatrics. 2013;132:28–36. [PubMed: 23733801]

17. Quinn N, Walls A, Milliken I, et al. Pyloric stenosis - do males and females present differently? Ulster Med J. 2011;80:145–147. [PubMed: 23526330]

18. Cascio S, Steven M, Livingstone H, et al. Hypertrophic pyloric stenosis in premature infants: evaluation of sonographic criteria and short-term outcomes. Pediatr Surg Int. 2013;29:697–702. [PubMed: 23686443]

19. Bertakis KD, Azari R, Helms LJ, et al. Gender differences in the utilization of health care services. J Fam Pract. 2000;49:147–152. [PubMed: 10718692]

20. Hunt-McCool J, Kiker BF, Chu Ng Y. Gender and the demand for medical care. Appl Econ. 1995;27:483–495.

21. Bosch F, Angele MK, Chaudry IH. Gender differences in trauma, shock, and sepsis. Mil Med Res. 2018;5:35. [PubMed: 30360757]

22. Magnotti LJ, Fischer PE, Zarzaur BL, et al. Impact of gender on outcomes after blunt injury: a definitive analysis of more than 36,000 trauma patients. J Am Coll Surg. 2008;206:984–991. [PubMed: 18471739]

23. Croce MA, Fabian TC, Malhotra TK, et al. Does gender difference influence outcome? J Trauma. 2002;53:889–894. [PubMed: 12435939]

24. Deitch EA, Livingston DH, Lavery RF, et al. Hormonally active women tolerate shock-trauma better than do men: a prospective study of over 4000 trauma patients. Ann Surg. 2007;246:447–453. [PubMed: 17717448]

25. Franconi F, Brunelleschi S, Steardo L, et al. Gender differences in drug drug responses. Pharmacol Res. 2007;55:81–95. [PubMed: 17129734]

**Table 1 –**

Complications associated with pyloromyotomy that were included in morbidity analysis as well as comorbidities adjusted for in statistical analysis.

| Complication category | Descriptions (ICD-9 Code) |
|---|---|
| Intraoperative | Accidental bowel puncture or laceration (998.2)<br>Hemorrhage (998.11)<br>Retained foreign body (998.4) |
| Gastrointestinal | Paralytic ileus (560.1)<br>Adhesal obstruction (560.81)<br>Enterostomy related (569.60)<br>Postoperative fistula (998.6) |
| Respiratory | Atelectasis (997.39)<br>Respiratory insufficiency (518.5)<br>Pneumothorax (512.1)<br>Pulmonary edema (518.4) |
| Cardiovascular | Cardiac complications resulting from a procedure (997.1)<br>Postoperative stroke (997.02)<br>Phlebitis or thrombophlebitis during or resulting from a procedure (997.2) |
| **Comorbidities adjusted for in statistical analysis** | **Descriptions (ICD-9 Code)** |
| History of prematurity | Extreme prematurity (765.0)<br>Prematurity (765.1) |
| Pulmonary disease | Postinflammatory pulmonary fibrosis (515)<br>Other alveolar or parietoalveolar pneumonopathy (516)<br>Other diseases of respiratory system (519)<br>Congenital anomalies of the respiratory system (748)<br>Respiratory distress syndrome (769)<br>Other respiratory conditions of fetus and newborn (770)<br>Symptoms involving respiratory system (786) |
| Congenital cardiac disease | Bulbus cordis and cardiac septal closure anomalies (745)<br>Other congenital anomalies of the heart (746)<br>Other congenital anomalies of the circulatory system (747) |

**Table 2 –**

Demographic information for males and females.

| Demographic | Total *n* = 48,834 | Male *n* = 39,953 | Female *n* = 8,881 | *P* - value |
|---|---|---|---|---|
| Age | | | | |
| ≥ 29 d | 35,388 (72.5%) | 27,817 (69.6%) | 6,661 (75.0%) | <0.01 |
| < 29 d | 13,446 (27.5%) | 12,136 (30.4%) | 2,220 (25.0%) | |
| Race | | | | |
| White | 23,117 (47.3%) | 19,027 (47.6%) | 4,090 (46.0%) | 0.03 |
| Black | 3,108 (6.4%) | 2,508 (6.3%) | 599 (6.7%) | 0.21 |
| Hispanic | 9,979 (20.4%) | 8,177 (20.5%) | 1,802 (20.3%) | 0.78 |
| Other | 2,992 (6.1%) | 2,425 (6.1%) | 567 (6.4%) | 0.38 |
| Missing | 9,638 (19.7%) | 7,816 (19.6%) | 2,969 (33.4%) | 0.14 |
| Comorbidities | | | | |
| Present | 2,890 (5.9%) | 2,075 (5.2%) | 815 (9.2%) | <0.01 |
| Operation day | | | | |
| Hospital day 1 | 12,783 (26.2%) | 10,642 (26.6%) | 2,142 (24.1%) | <0.01 |
| Region | | | | |
| Northeast | 7,420 (15.2%) | 6,049 (15.1%) | 1,371 (15.4%) | 0.55 |
| Midwest | 11,633 (23.8%) | 9,584 (24.0%) | 2,049 (23.1%) | 0.19 |
| South | 20,223 (41.4%) | 16,423 (41.1%) | 3,800 (42.8%) | 0.04 |
| West | 9,558 (19.6%) | 7,898 (19.8%) | 1,660 (18.7%) | 0.08 |

**Table 3 –**

Univariate analysis data for males and females.

| Outcomes | Total $n$ = 48,834 | Male $n$ = 39,953 | Female $n$ = 8,881 | $P$-value |
|---|---|---|---|---|
| Mortality (%) | 49 (0.10) | 20 (0.05) | 27 (0.30) | <0.01 |
| Total Complications (%) | 759 (1.6) | 590 (1.5) | 169 (1.9) | 0.02 |
| Cost in dollars (95% Confidence Interval) | 9123 (8536, 9709)* 5157 (5017, 52301)† | 8333 (7798, 8868)* 5075 (4937, 5217)† | 12666 (11026, 14306)* 5540 (5322, 5769)† | <0.01 |
| LOS in days (95% Confidence Interval) | 4.15 (3.92, 4.38)* 2.40 (2.35, 2.44)† | 3.72 (3.53, 3.90)* 2.33 (2.30, 2.38)† | 6.08 (5.44, 6.73)* 2.70 (2.60, 2.79)† | <0.01 |

*Arithmetic mean.

†Geometric mean.

**Table 4 –**

Results from the regression models[*] to evaluate the association with sex.

| Outcomes | Point estimate | Standard Error | 95% CI[†] | *P*-value |
|---|---|---|---|---|
| Mortality[‡] | | | | |
| Male | Reference | | | |
| Female | 3.26 | 1.26 | 1.52, 6.98 | <0.01 |
| Complications[‡,¶] | | | | |
| Male | Reference | | | |
| Female | 1.18 | 0.15 | 0.92, 1.50 | 0.19 |
| Cost[§] | | | | |
| Male | Reference | | | |
| Female | 1.05 | 0.01 | 1.02, 1.08 | <0.01 |
| Length of Stay[//] | | | | |
| Male | Reference | | | |
| Female | 1.28 | 0.05 | 1.18, 1.39 | <0.01 |

[*] Models were adjusted by age group, i.e. age in days <29 or >=29, race, complications, comorbidity, whether the surgeries were performed on the day of admission, and region with year fixed effect.

[†] Confidence Interval.

[‡] Point estimate and 95% CI are expressed as Odds Ratio.

[§] Hospital costs were log-transformed before the regression, and exponentiated point estimate and 95% CI are reported in the table.

[//] Point estimate and 95% CI are expressed as incidence rate ratio.

[¶] models were adjusted by age group, i.e., age in days <29 or >=29, race, comorbidity, whether the surgeries were performed on the day of admission, and region with year fixed effect.