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Factors Associated with Early Deaths Following Neonatal Male Circumcision in the United States, 2001-2010

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Abstract

We sought to quantify early deaths following neonatal circumcision (same hospital admission) and to identify factors associated with such mortality. We performed a retrospective analysis of all infants who underwent circumcision in an inpatient hospital setting during the first 30 days of life from 2001-2010 using the National Inpatient Sample (NIS). Over 10 years, 200 early deaths were recorded among 9,833,110 subjects (1 death per 49,166 circumcisions). Note: this figure should not be interpreted as causal but correlational as it may include both under-counting and over-counting of deaths attributable to circumcision. Compared to survivors, subjects who died following newborn circumcision were more likely to have associated co-morbid conditions, such as cardiac disease (OR: 697.8 [378.5-1286.6] p<0.001), coagulopathy (OR: 159.6 [95.6-266.2] p<0.001), fluid and electrolyte disorders (OR: 68.2 [49.1-94.6] p<0.001), or pulmonary circulatory disorders (OR: 169.5 [69.7-412.5] p<0.001). Recognizing these factors could inform clinical and parental decisions, potentially reducing associated risks.

Key words: circumcision, risks, death, complications, co-morbid conditions

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INTRODUCTION

Male circumcision is a surgery that removes part or all of the penile prepuce or foreskin.[1,2] In rare instances, the procedure is medically indicated, as in patients with recurrent, pathologic phimosis due to balanitis xerotica obliterans.[3,4] Most often, however, it is performed nontherapeutically on healthy newborns and other male minors.[5] In the United States, circumcision is typically performed by a physician shortly after birth. With an out-of-hospital rate of approximately 55% as of 2010,[6,7] such newborn male circumcision is the most common pediatric surgery performed in the USA.[8] With the exception of Israel, it is much less common in other Western developed nations.[9,10] It is the only pediatric surgery regularly performed on children who have not been diagnosed with a disease.

Like any surgery, circumcision carries risks. These include infection, bleeding, inflammation, development of fistulae or skin bridges, acquired torsion, buried penis, meatal stenosis, partial or complete penile amputation or other injury to the penis, and death.[11–13] Death is typically characterized as a rare complication of circumcision, insofar as the surgery is performed in a modern clinical setting by a well-trained provider.[14] However, precise estimates of death rates following such medicalized newborn circumcision have been notoriously difficult to establish. In this study, we attempt to provide a large-sample estimate of the frequency of early deaths (that is, deaths occurring during the same hospital admission) associated with newborn circumcision, along with an account of the major factors that are correlated with such mortality.

MATERIALS AND METHODS

Study Design and Description of Database

We performed a retrospective descriptive analysis of the Nationwide Inpatient Sample (NIS) for the years 2001 to 2010. The NIS is the largest all-payer inpatient database in the United States that provides information on close to 100 patient and hospital level variables during the index hospitalization.[15] NIS is a component of the Healthcare Cost and Utilization Project (HCUP) family of databases that include the State Inpatient Databases, Nationwide Emergency Department Sample, State Emergency Department Databases, Ambulatory Databases, and Hospital Re-admission Databases. The HCUP is sponsored by the Agency for Healthcare Research and Quality (AHRQ).

Up to the year 2010, the NIS database was designed such that approximately 20% of all acute care hospitals provided data. Each of the included hospitals provided information on 100% of hospitalizations that occurred in the selected years. Each hospitalization in the NIS database is assigned a discharge weight variable that can be used to project to nationally representative estimates of approximately all hospitalizations in the United States. Thus, the NIS can be used to examine close to 20 million hospitalizations occurring in the United States annually.[16] The NIS databases have been extensively validated and to date over 1000 publications have resulted from its analysis.[17] The NIS provides information on variables such as age, sex, race, insurance status, type of admission, co-morbid conditions, primary reason for hospitalization, procedures performed during hospitalization, disposition status, hospital charges, length of stay in hospital, type of hospital, geographic region of hospital, etc. The NIS has been designed to answer questions pertaining to health care utilization, health costs, and health outcomes, including those associated with uncommon conditions, procedures that are performed infrequently, or outcomes that are designated clinically rare events (such as death). Using single-center studies for examining these issues would be unviable owing to the lower statistical power with limited samples of data and a lack of generalizability or external validity.

Institutional Review Board (IRB) Approval

The present study used de-identified secondary datasets already in existence. The Office of Human Subjects Oversight Board at the University of Iowa deemed this project not to meet the regulatory definition of human subjects research and hence institutional review board (IRB) approval was not needed.

Subject Selection

Males with ages between 0 and 30 days who underwent a circumcision procedure were selected for inclusion in the present study. Circumcision procedures were identified by using ICD-9-CM procedure codes in the 15 procedure fields available in the database.[18] All subjects meeting these criteria were selected regardless of race, disposition status, or other related outcomes.

Key Variables

The following variables were examined in the present study.

Demographics: The demographic variables that were examined included race and insurance status (any governmental insurance programs, private insurance, or uninsured).

Co-morbid Burden: For each patient in the study cohort, the co-morbid burden severity was assessed using the NIS co-morbid severity files.[15] NIS severity files provide data on the presence of multiple comorbid conditions (deficiency anemias, rheumatoid arthritis/collagen vascular diseases, chronic blood loss anemia, congestive heart failure, chronic pulmonary disease, coagulopathy, diabetes [uncomplicated], diabetes [with complications], hypertension, liver disease, lymphoma, fluid and electrolyte disorders, metastatic cancer, neurological disorders, obesity, paralysis, peripheral vascular disorders, pulmonary circulation disorders, renal failure, solid tumor without metastasis, peptic ulcer disease excluding bleeding, valvular disease, and weight loss). For the purpose of this study, congestive heart failure, hypertension, and valvular disease were clustered as cardiovascular disease. The presence of different co-morbid conditions was coded as a binomial variable: “1” for presence of a specific co-morbid condition and “0” for absence of a specific co-morbid condition. In accordance with the data user agreement with HCUP-AHRQ, any individual cell count with ≤ 10 events was not reported. When such low cell counts were encountered, the term “DS” was used. “DS” refers to “discharge information suppressed.”

Hospital Characteristics: These included bed size of hospital (small, medium, or large bed-size hospitals as defined by HCUP-AHRQ), teaching status of hospital (teaching or non-teaching status as defined by the American Hospital Association), location of hospital (rural or urban location), and geographic region of hospital.[15]

Outcome: The outcome of interest in the present study was “early” or in-hospital death. Thus, for the purpose of this study, early circumcision deaths were deaths that occurred following the circumcision procedure but prior to discharge, that is, within the same hospital admission as the circumcision.

Analytical Approach

Simple descriptive statistics were used to summarize the data, including patient and hospital related variables. The descriptives were summarized by in-hospital mortality status. For computing nationally representative estimates, the discharge weight variable assigned to each hospitalization was used. The stratification unit was the stratum to which each hospital belonged. The stratum to which a hospital belonged was based on its geographic region (Northeast, Midwest, South, or West), locality (rural or urban), hospital ownership, teaching status of hospital, and bed size (number of beds in hospital based on geographic region and location). Descriptive statistics were computed using SAS Version 9.4, SAS Callable SUDAAN Version 11.0.1, and SigmaPlot Version 13.0 software.

RESULTS

During the study period, we identified 9,833,110 subjects who underwent a circumcision procedure within the first 30 days of life in an inpatient hospital setting. Among these, there were 200 deaths within the same hospital admission as the procedure, or 1 death occurring shortly after every 49,166 circumcisions (10.2 deaths per 500,000 circumcisions). The distribution of early circumcision deaths per study year is shown in Table 1.

Subjects who died soon after circumcision were predominantly white (63.9%), and had medical care funded by private insurance (52.1%) or Medicaid (39.7%) (Table 2). Most deaths occurred at teaching hospitals (80.1%), large bed-size hospitals (59.6%), and those predominantly located in the South (33.8%) or Midwest (33%) (Table 3).

The most prevalent co-morbid conditions for this sample are shown in Table 4. Compared to survivors, subjects who died soon after being circumcised were significantly more likely to have associated co-morbid conditions. The presence of cardiovascular comorbidities was associated with significantly greater odds of death (OR: 102.9 [61.7 – 171.5] p<0.001). Likewise, the presence of coagulopathy (OR: 159.6 [95.6-266.2] p<0.001), fluid and electrolyte disorders (OR: 68.2 [49.1-94.6] p<0.001), pulmonary circulatory disorders (OR: 169.5 [69.7-412.5] p<0.001), and neurological disorders (OR: 111.7 [45.9 – 271.6] p<0.001), were significantly associated with greater odds of death following circumcision.

DISCUSSION

Data from this large national cohort of infants who underwent circumcision in an inpatient hospital setting in the first 30 days of life can help to inform estimates of the risk of early death following this procedure, especially in patients with co-morbid conditions. In the present analysis, we identified 1 early death for every 49,166 newborn inpatient circumcisions, or 10.2 early deaths per 500,000 newborn inpatient circumcisions. We stress that this figure refers to deaths that occurred subsequent to the circumcision but prior to discharge within the same hospital admission; it should not be taken to refer to the frequency of deaths *caused* by newborn circumcision, as the present data cannot directly support such an inference. To see this, consider the following hypothetical cases:

> Case A. Infant Adam is a seemingly healthy newborn infant who has a ritual circumcision performed as an outpatient. He develops severe bleeding immediately following the procedure, and is transferred to the local hospital where he requires multiple blood transfusions. Unfortunately, he does not respond to treatment and dies two days later. Tests later confirm that he had hemophilia.
>
> Case B. Infant Ben is thought to be a healthy newborn delivered by cesarean section and has a circumcision on the first day of life. On day 3, he develops refractory shock and dies. An autopsy reveals an undiagnosed ductal-dependent cardiac lesion (interrupted aortic arch).
>
> Case C. Infant Charlie is circumcised in the first days of his life in a hospital inpatient setting, but suffers a severe hypoxic-ischemic brain injury due to cardiorespiratory arrest that occurred during the procedure. Six years later, still with severe neurologic sequelae, Charlie dies from acute respiratory failure following aspiration pneumonia.
>
> Case D. Infant David is circumcised in the first days of his life in a hospital inpatient setting, but suffers a complication: too much skin is removed, leaving a tight scar around his penis, ultimately preventing urination. A month later, David is re-admitted to the

hospital for a correction surgery to relieve his urethral obstruction, but dies due to complications from anesthesia.

In the case of Adam, the death would be appropriately causally attributed to the newborn circumcision in conjunction with undetected hemophilia; however, Adam's death would not be included in our data set since the circumcision itself was performed in an outpatient setting whereas we looked only at data from inpatient circumcisions (according to a recent study, between 1970 and 1996, an average of 45.4% of all circumcisions were non-hospital based or post-discharge, i.e., "unrecorded").[19,20] Adam, then, would be an instance of undercounting a death due to newborn circumcision for our purposes.

By contrast, Ben would be an instance of overcounting such a death: although he died during the same hospital admission as his circumcision, and would thus be included in our data set, it would not be appropriate to causally attribute the death to the circumcision, because of the significant confound of the undiagnosed cardiac defect.

Finally, Charlie and David, like Adam, would also represent cases of undercounting: both deaths are plausibly attributable to circumcision, in that, had the circumcision not occurred, neither would the deaths from the more immediate causes[21] (although this is less certain in the case of Charlie). However, the deaths occurred sometime after the original hospital discharge and so would not be included in our data set.

To summarize, our figure of 10.2 early deaths per 500,000 newborn inpatient circumcisions may (1) include some deaths that were not caused by such circumcision, as well as (2) exclude some deaths that were caused by such circumcision. It is not possible to determine how many instances of each of these is represented in our data set. However, it must be emphasized that our data do not cover outpatient, post-discharge, or ritual circumcisions, which, as noted, may make up nearly half of all US circumcisions. Thus, any deaths caused by such circumcisions are invisible to our study. This makes it likely that we have underestimated the total number of deaths associated with newborn circumcision in the United States during the study period. With these important caveats in mind, we ask: How does our figure compare with the previous estimates?

Prior death estimates

In 1953, Speert reported 1 death from newborn circumcision over the period 1939-1951, based on records from the New York City Health Department.[22] The total number of newborn circumcisions during this period was unknown, but based on the assumption of a 61.27% circumcision rate (the rate observed at a single hospital, Sloane Hospital, generalized to all hospitals in New York City) and the further assumption that this rate remained constant over the 12 year period, Speert estimated 1 operative death per 566,483 newborn circumcisions (i.e., 61.27% of the 924,569 known live male births in New York City). This corresponds to <1 death per 500 000 newborn circumcisions; the death was attributed to fatal hemorrhage following a ritual circumcision performed at-home by a Jewish *mohel*. The limitations of this estimate include: (1) it is more than six decades old, and (2) its denominator is based on an extrapolation from 1 hospital combined with data from a single city. Therefore, generalizability may be limited.

In 1982, King reported in a commentary that 500,000 consecutive neonatal circumcisions were performed over an unidentified period of time in New York City without any fatalities, which entails less than 1 death per 500,000 circumcisions.[23] As with the Speert estimate, this figure concerns a single city, and therefore cannot speak to death rates elsewhere, much less nationally. In addition, King did not provide any references for his claim, including who performed the circumcisions, in what setting, with what instruments, etc., rendering it difficult to interpret. In fact, it is possible that King was simply alluding to the earlier study by Speert from nearly 30 years earlier.

In 1989, Wiswell and Geschke reported no deaths from circumcision during the first month of life over a series of 100,157 circumcisions performed at US Army hospitals between 1980 and 1985.[24] The authors acknowledge that an unknown number of circumcised boys may have later been admitted to a civilian hospital, in which case any complications or deaths would not have been included in their records review. There is also uncertainty about the extent to which such findings can be generalized to non-Army hospitals during the period in question. Finally, the estimate is more than three decades old.

In 2010, based on an analysis of US hospital discharge records, Bollinger estimated that 117 deaths related to newborn circumcision occurred in the United States in 2007 out of a total of 1,299,000 circumcisions estimated to be performed that year. This amounts to 9.01 deaths per 100,000 circumcisions or 45.03 deaths per 500,000 circumcisions—far higher than the earlier estimates as well as our own.[25] However, Bollinger's figure included deaths that occurred during the entire neonatal period, up to 28 days of life. When only "early" deaths are included—that is, deaths occurring prior to hospital release, as in our study—Bollinger's estimate drops to 14.5 deaths per 1,299,000 circumcision procedures, or 5.6 deaths per 500,000 circumcisions, a figure that is more closely aligned with ours.

Morris et al. have critiqued the estimate by Bollinger, arguing that he must have mistakenly assumed that sex differences in infant mortality in the United States are entirely due to newborn circumcision, when in fact similar sex differences occur in countries with low rates of such circumcision.[26] However, Morris et al. appear to have misinterpreted the report by Bollinger. While Bollinger does refer to a 40.4% relative higher death rate for infant males compared to infant females in the United States, this is not reported as an overall relative death rate, but rather one "from causes that are associated with male circumcision complications, such as infection and hemorrhage," specifically during the period of "one hour after birth to hospital release (day 2.4), the time frame in which circumcisions are typically performed."

Constraints on estimation

One of the major challenges in estimating the number of deaths in which newborn circumcision is likely to have played a contributory role is that death certificates typically fail to mention the underlying condition or procedure that led to the subject's death, and instead list only the immediate cause of death such as exsanguination or overwhelming sepsis.[27] For example, a study of children with heritable disorders who died while in a pediatric intensive care unit showed that that the underlying disorder was left off the death certificate 41% of the time.[28]

Adding to the challenge is a lack of adequate record-keeping in countries where newborn circumcision remains customary. For example, if complications are treated in a hospital or clinic other than the one in which the original circumcision was performed, the general inability to cross-link register data in countries such as the United States that do not have a unique medical ID for every citizen can make it difficult or impossible to confirm that the complications were in fact circumcision-related.[29]

Yet another problem is "the natural tendency of physicians not to ascribe a poor outcome to an elective procedure," which may lead to "gross underestimates" of the frequency of life threatening infectious complications from circumcision.[30] In support of this view, Cleary and Kohl draw attention to a significant gap in the relevant data (internal references omitted):

> In one retrospective series of more than 900,000 male births, there were no deaths attributed to infection. The incidence of neonatal sepsis is estimated at 1:300 to 1:1,600 live births. With the usual male predominance (approximately 2:1), one might have expected between 700 and 3,900 in this large study. Since the rate of circumcision during the years of study was 61%, there must have been many males who were circumcised and who became septic but in whom the two events were not judged to have been related.[30]

According to the American Academy of Pediatrics (AAP), the "true incidence" of surgical complications attributable to newborn circumcision is unknown.[6] This lack of certainty is due to disagreements about appropriate diagnostic criteria for certain complications as well as other limitations with existing data, such as those described above.[31] Other risks, including risks to the developing nervous system and long-term risks to neuroendocrine and immune system stress responses are even less well-studied.[32] These issues should be a priority for future research.[33]

Limitations

Our study has several limitations inherent to its retrospective design, including the lack of granularity involving patient-level observations that is typical of a large de-identified dataset. Nevertheless, we believe that the use of a large multi-year national dataset was the only way to capture this relatively rare outcome that may follow neonatal male circumcision along with its associated factors. We chose to include a more remote (2001 to 2010) sample to decrease the likelihood that one could attempt to re-identify low prevalence events from this de-identified sample. In addition, the NIS data sampling strategy was constant between 2001 and 2010, changing in 2012 and once again in 2015 with the implementation of ICD 10 codes.

Another obvious limitation of our study is that it lacks a control group of intact (non-circumcised) newborns, which would not have been possible given the design of the study.

Including intact neonates as a control group would have captured deaths that occurred in children with severe co-morbidities that were deemed too ill to undergo circumcision, but who otherwise would have been circumcised, or children with non-survivable malformations and those for whom life support measures had been limited. In this context, it should be noted that circumcision is typically performed only when the physician or other operator believes that the newborn is stable and healthy enough to undergo surgery. Such judgments are of course sometimes mistaken, for example when proper screening is not undertaken. However, an infant that has been deemed to be in sufficiently good health to be operated on, and then dies shortly after the operation, is relatively unlikely to be one with sufficiently severe co-morbidities that these would independently explain his death without the operation. Thus, although we emphasize once again that our findings should be taken as correlational rather than causal, it is clear that baby boys can and do die as a result of their circumcision procedures, including in hospital settings.[34–44]

Co-morbidities

In keeping with the correlational nature of our results, we observed a significant increase in the odds of death following circumcision in children with certain co-morbidities, including cardiac disease, coagulopathy, fluid and electrolyte disorders, and pulmonary circulatory disorders. Many, if not all of these co-morbidities can be identified *a priori* in neonates and their presence should inspire caution as to whether these more vulnerable neonates are indeed able to tolerate this particular surgical procedure and its attendant consequences (for example, pain and related sequelae).[45–48] Pending further research, we suggest that the specific co-morbidities we have identified in this study should be considered as potential contra-indications for newborn circumcision.

CONCLUSION

In this study, using a validated multi-year national dataset, we identified 1 early death for every 49,166 newborn inpatient circumcisions, or 10.2 deaths per 500,000 newborn inpatient circumcisions; however, this figure cannot be simply interpreted as a causal relationship, since our study design allows for both undercounting and overcounting of deaths due to such circumcisions and we do not know the true proportion of over-counted versus under-counted deaths.

In addition, we identified a number of co-morbid conditions that were associated with a significant increase in the odds of death following newborn circumcision, and we have suggested that these may need to be considered as potential contra-indications for the surgery pending further research.

According to the AAP, repeated exposure to painful stimuli soon after birth can cause immediate and long- term adverse outcomes, including physiologic instability and altered brain development, as well as abnormal somatosensory and stress response systems, which can persist into later childhood.[48] The AAP therefore recommends that “every health care facility caring for neonates should implement a pain-prevention program that includes strategies for minimizing the number of painful procedures performed."[48] Since newborn circumcision is a surgical procedure that inevitably causes pain as well as carries other risks, up to and including death, and since it is performed on a healthy subject who does not require surgery on medical grounds, it is a clear candidate for a procedure whose incidence should be minimized, all things considered.

In this context, it should be remembered that the disvalue of any given risk is a function of its likelihood as well as its magnitude, which is in turn affected by which alternative courses of action are available.[49] While the most common surgical risks associated with circumcision, such as pain, bleeding, or infection may be considered tolerable when a surgery is medically necessary, their disvalue to an individual is much greater when he is healthy and does not require surgery.[50] In addition, while other risks associated with circumcision may be less common, they may also be extremely serious—as in the case of death—and must therefore be weighted more heavily in assessments of the value or disvalue of performing the surgery.[51]

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Author contributions

BDE drafted the Introduction and Discussion sections as well as revised the entire manuscript. VA and VA carried out and reported all data analyses and revised the entire manuscript. ATR drafted the Methods and Results sections and revised the entire manuscript.

Disclosure

None.

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FIGURES AND TABLES

Table 1. Annual distribution of early deaths following neonatal circumcision

Year of Hospitalization	Dead n= 200	Alive n= 9,832,910
2001	DS	938,253 (9.5%)
2002	28 (14%)	991,608 (10%)
2003	DS	952,707 (9.6%)
2004	33 (16.5%)	962,683 (9.7%)
2005	21 (10.5%)	987,666 (10%)
2006	20 (10%)	997,218 (10.1%)
2007	26 (13%)	1,031,720 (10.4%)
2008	15 (7.5%)	1,012,361 (10.2%)
2009	15 (7.5%	973,589 (9.9%)
2010	36 (18%)	985,105 (10%)

DS = Discharge information suppressed due to low cell count (as per data user agreement with AHRQ)

Table 2. Insurance status and demographic information

		Dead n= 200	Alive n= 9,832,910
Race	White	96 (48%)	4,450,060 (45.3%)
	Black	30 (15%)	1,049,500 (10.7%)
	Hispanic	DS	408,820 (4.2%)
	Asian/Pacific Islander	DS	274,481 (2.8%)
	Native Americans	DS	46,288 (0.5%)
	Other Races	DS	293,779 (3%)
	Missing race information	50 (25%)	3,309,982 (33.7%)
Insurance status	Medicare	DS	19,635 (0.2%)
	Medicaid	80 (40%)	3,112,608 (31.7%)
	Private	104 (52%)	6,031,235 (61.3%)
	Self-Pay	DS	369,369 (3.8%)
	Other insurance	DS	279,114 (2.8%)
	Missing insurance information	DS	20,949 (0.2%)

DS = Discharge information suppressed due to low cell count (as per data user agreement with AHRQ)

Table 3. Hospital characteristics

		Dead n= 200	Alive n= 9,832,910
Bed size	Small	30 (15%)	1,139,914 (11.6%)
	Medium	50 (25%)	2,512,696 (25.6%)
	Large	120 (60%)	6,131,148 (62.4%)
	Missing data	-	49,152 (0.5%)
Hospital region	Northeast	26 (13%)	1,972,353 (20.1%)
	Midwest	66 (33%)	3,551,793 (36.1%)
	South	67 (33.5%)	2,842,030 (28.9%)
	West	40 (20%)	1,466,734 (14.9%)
	Missing data	-	-
Hospital teaching status	Non-teaching	40 (20%)	4,903,235 (49.9%)
	Teaching	160 (80%)	4,880,522 (49.6%)
	Missing data	-	49,153 (0.5%)

Table 4. Co-morbid condition and odds of death following circumcision

	Dead n= 200	Alive n= 9,832,910	Odds Ratio (95% CI)
Cardiovascular disease	16 (8%)	8,304 (0.084%)	102.9 (61.7 – 171.5)
Coagulopathy	16 (8%)	5,355 (0.054%)	159.6 (95.6 – 266.2)
Fluid and electrolyte disorders	47 (23.5%)	44,090 (0.448%)	68.2 (49.1 – 94.6)
Pulmonary circulatory disorders	DS	1,487 (0.015%)	169.5 (69.7 – 412.5)
Neurological disorders	DS	2,257 (0.023%)	111.7 (45.9 – 271.6)

DS = Discharge information suppressed due to low cell count (as per data user agreement with AHRQ)