



## RESEARCH REPORT

# A retrospective cohort study of adverse event assessment during anesthesia-related procedures for cochlear implant candidacy assessment and cochlear implantation in infants and toddlers

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## Abstract

**Background:** Cochlear implantation in children with sensorineural hearing loss is preferably performed at youngest age because early auditory input is essential to prevent neural plasticity decline. In contrast, the rate of anesthetic adverse events is increased during infancy. Therefore, to provide recommendations regarding an optimal pediatric implantation age, these possible anesthetic risks in infants need to be taken into account.

**Aims:** This study aimed at assessing the relation between the age at cochlear implant surgery and anesthetic and surgical adverse events. Secondary aims were to evaluate anesthetic and surgical adverse events in relation to (a) the number of preoperative anesthesia-related procedures for cochlear implant candidacy assessment and (b) the anesthetic maintenance agent (total intravenous anesthesia versus inhalation anesthesia) during implantation.

**Methods:** We executed a retrospective cohort study to evaluate cochlear implantation performed in infants and toddlers between January 2008 and July 2015 in a tertiary pediatric center. We compared anesthetic and surgical adverse events between age-at-implantation (0-12 and 12-24 months of age) groups. Furthermore, we assessed whether anesthetic adverse events occurred during preoperative anesthesia-related procedures for cochlear implant candidacy assessment.

**Results:** Forty-six cochlear implantations were performed in 43 patients requiring 42 preoperative anesthesia-related procedures. Nineteen cochlear implantations (41.3%) were performed during infancy. During implantation, the maintenance agent was either sevoflurane (n = 22) or propofol (n = 24). None of the patients encountered major anesthetic adverse events, whereas minor adverse events occurred during 34 cochlear implantations. Those attributed to surgery occurred following six implantations. Neither the age at implantation nor the anesthetic maintenance agent was significantly related to the occurrence of both types of adverse events.

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**Conclusions:** Adverse events occur independent of the age at implantation, the number of anesthetic preoperative procedures, and the type of anesthetic maintenance agent in patients who received a cochlear implant before 24 months of age.

**KEYWORDS**

anesthesia, child, cochlea, cochlear implantation, infant, sensorineural hearing loss

## 1 | INTRODUCTION

Children with profound sensorineural hearing loss are provided with cochlear implants (CI) when their speech and language development does not develop sufficiently following a hearing-aid trial. Exposure to auditory input during the first year of life is essential to prevent neural plasticity decline that could delay language development.<sup>1</sup> Scheduling cochlear implantation during this critical period of cortex neuroplasticity is essential; therefore, most otologists currently advocate implantation during infancy or early childhood.<sup>1</sup>

From a surgical perspective, CI surgery is considered a safe procedure with low rates of surgical adverse events, which occur irrespective of the age at implantation.<sup>2-4</sup> Previous studies report that surgical adverse event rates can incur from 3.2%<sup>2</sup> to 24.7%<sup>3</sup>; dispersion in these adverse event rates can be explained by different adverse events definitions and results from application of different surgical techniques. Due to these relatively low rates, consensus exists that CI surgery can be performed safely during infancy.<sup>2,3</sup> Although CI surgery might seem safe in infants from a surgical perspective, it could result in more anesthetic risks. Firstly, multiple preoperative anesthetic procedures are required during diagnostic workup for CIs (eg, magnetic resonance imaging (MRI) scan), which could induce a negative cumulative anesthetic effect during CI surgery. Furthermore, children, especially infants, suffer from relatively higher rates of anesthetic adverse events compared to adults (4.6% and 1.2% respectively).<sup>5,6</sup> Thirdly, exposure to anesthesia during infancy could lead to an increased risk of poor neurodevelopmental outcome during (long-term) follow-up.<sup>7,8</sup> Therefore, understanding these anesthesia-related risks could provide crucial information to be able to define the optimal age for pediatric CI surgery.<sup>3</sup>

Moreover, the anesthesia maintenance type during CI surgery could affect the occurrence of perioperative adverse events. For example, propofol can lower the amount of perioperative blood loss (ie, through its hypotensive or vasodilatory actions, it can lower the amount of perioperative bleeding) resulting in optimized visualization of anatomical structures during surgery.<sup>9</sup> Therefore, some surgeons prefer propofol maintenance anesthesia over sevoflurane.<sup>9</sup> Furthermore, propofol maintenance anesthesia has another advantage over sevoflurane as it is associated with a lower risk of perioperative laryngospasm in children.<sup>10</sup>

Although consensus exists that CI surgery can be performed safely during infancy from a surgical perspective,<sup>2,3</sup> most surgeons refrain from performing CI surgery during (early) infancy due to the aforementioned anesthetic risks. We aim to define the optimal

### Clinical implications

- A Previous research demonstrates that adverse events during cochlear implant surgery occur irrespective of the age of infants and toddlers undergoing surgery.
- B Results showed that both surgical and anesthetic adverse events occurred independently of: the age at implantation, the number of preoperative anesthesia-related procedures for cochlear implant candidacy assessment and the type of anesthetic maintenance agent in ASA 1 or 2 patients implanted before 24 months of age. Therefore, the optimal pediatric cochlear implantation age could be directed toward infants.

age for CI surgery incorporating the surgical and anesthetic risks. Therefore, we assessed the occurrence of anesthetic and surgical adverse events during the CI surgery in relation to the age at surgery. Furthermore, we assessed whether (a) the number of preoperative anesthesia-related procedures for CI candidacy assessment and (b) the anesthetic maintenance agent (total intravenous anesthesia (TIVA) versus inhalation anesthesia) affected adverse event occurrence.

## 2 | MATERIALS AND METHODS

### 2.1 | Study design and participants

In this retrospective cohort study, we included all infants and toddlers who received a CI between January 2008 and July 2015 in a tertiary hospital (Wilhelmina Children's Hospital, University Medical Centre Utrecht, The Netherlands). We assessed the occurrence of anesthetic and surgical adverse events during both (a) all preoperative anesthesia-related procedures for CI candidacy assessment and (b) the CI surgery. Bilateral simultaneous cochlear implantations were assessed as one CI surgery. Sequential and CI revision surgeries were included as separate CI surgeries. We subdivided included CI surgeries into two groups: surgery performed in infants (before 12 months) and in toddlers (between 12 and 24 months of age), a subdivision that is in line with previous studies evaluating adverse events during CI surgery.<sup>2-4</sup>

Indication for CI surgery was decided upon a multidisciplinary meeting and based on both the Brainstem Evoked Response Audiometry (BERA) result and the clinical outcome of a 12-week obligatory hearing-aid trial. This multidisciplinary CI team includes audiologists, speech and language therapists, social workers, and otologists. One otologist from this team performed all CI surgeries.

Results are reported in line with STROBE guidelines.<sup>11</sup>

## 2.2 | Variables

The following baseline characteristics were collected: gestational age (prematurity defined as birth before 37 weeks of pregnancy), age at implantation, gender, preoperative weight, hearing loss etiology, comorbidities, number of preoperative anesthetic procedures, CI side, recent respiratory tract infections (occurrence: <2 weeks preoperatively), and American Society of Anesthesiologists (ASA) classification. We documented all perioperative and postoperative drugs that were administered. The following time periods were registered: operating room (OR) time (general anesthesia duration; in minutes), postanesthesia care unit (PACU) time (PACU admission until PACU discharge; in minutes), time to discharge (defined as: PACU discharge until hospital discharge; in days), and follow-up (defined as: hospital discharge until last recorded visit; in years).

## 2.3 | Anesthesia protocol for implantation

In line with World Health Organization (WHO) standards, all CI surgeries started with a surgical briefing and time-out procedure. Parents decided whether patients received anesthetic induction through intravenous (iv) propofol or sevoflurane inhalation. Orotracheal intubation was performed following administration of sufentanyl (0.1–0.3 mg/kg) and a standard dose of muscle relaxation (atracurium 0.5–0.7 mg/kg or mivacurium 0.2 mg/kg). Since this muscle relaxation has a short duration of action, there is no perioperative interference with facial nerve monitoring. The pediatric-trained anesthesiologist defined the type of maintenance anesthetic drugs (TIVA or sevoflurane inhalation) and intraoperative pain treatment (remifentanyl or sufentanyl). The surgeon infiltrated the retro-auricular region perioperatively with lidocaine (xylocaine 1% with epinephrine 1:80,000). Postoperative analgesia included paracetamol (iv 15 mg kg<sup>-1</sup> 6 hr<sup>-1</sup>), combined with diclofenac in patients older than 6 months (iv 1 mg kg<sup>-1</sup> 8 hr<sup>-1</sup>), and, on indication, additional morphine (iv 0.1 mg/kg bolus and 0.25 mg kg<sup>-1</sup> 24 hr<sup>-1</sup> continuously). Perioperative standard monitoring contained: an electrocardiogram, pulse oximetry, noninvasive blood pressure, facial nerve monitoring, and temperature measurement. All patients were positioned on a heating mattress (38°C) and covered with a heating blanket (42°C) to maintain the core temperature between 36.5 and 37.5°C.

## 2.4 | Adverse event classification

Anesthetic adverse events were classified into major (stroke, cardiac arrest, sepsis, re-intubation, and death<sup>2</sup>) and minor adverse events (respiratory (laryngospasm and/or bronchospasm), gastrointestinal (nausea, vomiting, diarrhea), fever ( $\geq 37.5^\circ\text{C}$ ; present until the third day postoperatively), excessive pain, skin reaction, facial edema, and nosebleeds). Three data sources were assessed for adverse event occurrence during the hospital stay of the patient: electronic patient charts, anesthetic records (Anesthesia Information and Management System (AIMS)), and postoperative nursing reports.<sup>12</sup>

Furthermore, we assessed the selected surgical technique (mastoidectomy with posterior tympanotomy approach, suprameatal or endaural approach) and perioperative and postoperative major (meningitis or CI infection needing surgical intervention) and minor (skin erythema or infection, acute otitis media (AOM), vertigo, CI device failure needing re-intervention) surgical adverse events occurring within 30 days postoperatively (surgical adverse events directly related to the CI surgery) and long-term surgical adverse events (occurrence more than 30 days following the CI surgery).

## 2.5 | Statistical methods

Data were analyzed using IBM SPSS statistics software package (IBM® SPSS® Statistics version 21, IBM Corp.). Significance was set to a *P*-value of .05. The Shapiro-Wilk test was used to confirm non-normal data distribution. The Mann-Whitney *U* test was used to perform comparisons between the two age-at-implantation groups when data were not normally distributed. Nonparametrical tests were used to assess the relations between dichotomous variables: we used either the chi-square test or Fisher's exact test when the variable occurred ten times or less.

Backward logistic regression was used to evaluate whether the occurrence of anesthetic adverse events during the CI surgery was influenced by: preoperative weight, the age at surgery, the number of preoperative anesthetic procedures related to CI assessment, the anesthetic maintenance technique, and diclofenac administration. A separate backward logistic regression analysis was performed to assess whether one of the following variables affected the occurrence of a surgical adverse event during the CI surgery: preoperative weight, the age at surgery, the anesthetic maintenance technique, and the surgical technique. Due to the explorative nature of this study and the limited sample size, a *P*-value of  $\leq .05$  was considered to be significant during these regression analyses.

## 3 | RESULTS

### 3.1 | Participants

Forty-two preoperative CI candidate assessment procedures were performed under general anesthesia: 19 procedures to perform CT

scans, 13 to perform MRI scans, four to perform both a CT and MRI scan, two to perform BERA and a CT scan, two to perform BERA and tympanostomy tube placement, and two to perform BERA and microscopic ear inspection (Table 1). One infant and two toddlers experienced laryngospasm during CI candidacy assessment procedures (one MRI scan, one CT scan, and one CT scan combined with BERA) (*data not shown*).

Forty-six CI surgeries were performed in 43 pediatric patients (Table 1). An additional CI surgery was included of three selected patients (one sequential CI surgery in a toddler and two CI revision surgeries in an infant and a toddler), which explains the discrepancy between inclusion of 43 pediatric patients and the 46 performed CI surgeries. The revision cases included: one simultaneously implanted patient who was explanted unilaterally due to infection and successfully re-implanted following antibiotic treatment, and a

re-implantation following ex-plantation of an incomplete CI electrode placement due to cochlear ossification resulting from meningitis.

Hearing loss etiology of the included patients entailed: postmeningitis ( $n = 7$ ), connexin 26 mutation ( $n = 3$ ), cytomegalovirus (CMV) infection ( $n = 4$ ), syndrome related ( $n = 5$ ), and unknown etiologies ( $n = 24$ ).

Fourteen (33%) patients had comorbidities that entailed: epilepsy ( $n = 2$ ), metabolic disorders ( $n = 2$ ; antibody synthesis defect and hyperbilirubinemia), neurological pathology ( $n = 3$ ; encephalopathy, cerebral infarction, psychomotor retardation), and various syndromes ( $n = 7$ ; Waardenburg ( $n = 2$ ), Usher, Emanuel, Jervell-Lange-Nielsen, Beckwith-Wiedemann, 7q11.23 duplication). Table 2 shows the applied surgical and anesthetic techniques in our cohort.

Anesthetic adverse events did not significantly vary between age-at-implantation groups (Table 3). Furthermore, propofol

Age-at-implantation group	CI < 12 mo.	CI 12-24 mo.	Total (% of total)
No. of patients	18	25	43
Total number of anesthetic procedures related to CI surgery	33	55	88
Total number of CI surgeries	19	27	46
Total number of preoperative anesthetic procedures related to CI candidacy assessment	14	28	42
Number of preoperative anesthetic procedures related to CI assessment per individual cochlear implanted patient [range]	1 [0-2]	1 [0-3]	1 [0-3]
<b>Baseline characteristics</b>			
Females (% of no. of patients per age group)	7 (39%)	16 (64%)	23 (53%)
Preoperative weight (kg in mean) (SD)	8.7 ± 1.4	10.4 ± 1.8	9.5 ± 1.8
Preoperative respiratory tract infection (% of no. of patients per age group)	7 (39%)	7 (28%)	14 (33%)
Year of birth [range]	2007-2014	2007-2014	2007-2014
Age at surgery (median in years) [IQR]	0.79 [.3]	1.19 [.6]	1.03 [.5]
ASA I: II (no. of patients per age group)	14:4	17:8	31:12
Prematurity	0	4 (16%)	4 (9%)
Comorbidities (% of no. of patients per age group)	4 (22%)	10 (40%)	14 (33%)
<b>Duration of hospitalization + follow-up</b>			
OR time [IQR]	267 [84]	257 [132]	259.5 [116.8]
PACU time [IQR]	64 [32]	60 [36]	60.5 [34.8]
Time to discharge [IQR]	2.1 [1.1]	1.9 [.3]	1.9 [.95]
Follow-up time [IQR]	3.6 [3.82]	4.1 [3.1]	3.38 [3.6]

**TABLE 1** Baseline characteristics of 46 included CI surgeries performed in 43 patients, arranged according to age-at-implantation groups

Abbreviations: ASA, American Society of Anesthesiologists; CI, Cochlear Implant; IQR, interquartile range; kg, kilograms; min., minutes; n.a., not applicable; no., number; OR, operating room; PACU, postanesthesia care unit; SD, standard deviation.

**TABLE 2** Surgical and anesthetic techniques used during the 46 CI surgeries performed in 43 patients, arranged according to age-at-implantation groups

Age-at-implantation group	CI < 12 mo.	CI 12-24 mo.	Total (% of total no. of surgeries)
Unilateral vs bilateral implantation			
Unilateral (Left): Unilateral (Right)	0:5 (26%)	7 (26%): 5 (19%)	17 (37%)
Simultaneous implantation	14 (74%)	15 (56%)	29 (63%)
CI surgical techniques			
MPTA: SMA	6 (32%): 11 (58%)	9 (33%): 14 (52%)	46 (100%)
Endaural approach	1 (5%)	0	1 (2%)
Combined	0	3 (11%)	3 (7%)
MPTA (revision) surgery	1 (5%)	1 (4%)	2 (4%)
Anesthetic techniques			
Sevoflurane: Propofol	15 (79%): 4 (21%)	7 (26%): 20 (74%)	46 (100%)
Sufentanil	15 (79%)	16 (59%)	46 (100%)
Remifentanyl	6 (32%)	21 (78%)	46 (100%)
Morphine	17 (90%)	24 (89%)	41 (89%)
Perfalgan	18 (95%)	26 (96%)	44 (96%)
Diclofenac	7 (37%)	21 (78%)	28 (61%)
Perioperative administered muscle relaxers: Atracurium: Mivacurium: none	12 (63%): 0:7 (37%)	19 (70%): 2 (7%): 6 (22%)	31 (67%): 2 (4%): 13 (28%)
Perioperative administered antibiotics: Augmentin: Cefazolin	19 (100%): 0	23 (85%): 4 (15%)	46 (100%)
Perioperative administered anti-emetics			
None	10 (53%)	12 (44%)	22 (48%)
Ondansetron	3 (16%)	12 (44%)	15 (33%)
Dexamethasone	5 (26%)	3 (11%)	8 (17%)
Ondansetron + Dexamethasone	1 (5%)	0	1 (2%)

Note: Endaural approach, a direct transcanal cochleostomy, following electrode insertion the lead is placed in a channel drilled in the posterior wall. This approach does not require a mastoidectomy.

Abbreviations: CI, cochlear implant; mo., months; MPTA, mastoidectomy with posterior tympanotomy approach; n.a., not applicable; no., number; SMA, suprameatal approach.

maintenance administration did not result in relatively less perioperative bleeding or respiratory events than sevoflurane administration.

Surgical adverse events occurred on average after 11.16 days (SD: 3.58). The occurrence of a surgical adverse event was not affected by the age at implantation (Table 3). A toddler who developed AOM and fever 3 days postoperatively was suspected of meningitis. Although cultures remained negative, a 10-day ceftriaxone and vancomycin treatment was administered, which is in accordance with our meningitis protocol. The fever resolved and no long-term meningitis sequelae are currently present.

The long-term (>30 days) major events entailed two infants and one toddler undergoing ex-plantation due to infection occurring on average 0.84 years (SD: 0.62) following surgery. The minor long-term events included two hard CI failures needing intervention: one soft-ware and one traumatic failure occurring on average 2.28 years (SD: 1.97) following surgery.

Regression analyses showed that none of the selected variables affect the occurrence of either an anesthetic or a surgical adverse event during the CI surgery (Table S1).

## 4 | DISCUSSION

Definition of the optimal age for CI surgery is balancing between implantation at the youngest age to allow optimal speech and language development and the increased risk of (anesthetic and surgical) adverse events during infancy. The present multidisciplinary study confirms that (a) there were no measured differences in the incidence of adverse events during CI surgery in infants compared to toddlers, (b) multiple preoperative anesthetic procedures for CI candidacy assessment did not result in a negative cumulative anesthetic effect during CI surgery, and 3) TIVA did not result in a superior surgical field and less perioperative laryngospasm compared to sevoflurane maintenance administration.

Four other pediatric CI studies<sup>2-4,13</sup> confirm that anesthetic adverse events occur irrespective of the age of the pediatric patients undergoing surgery. Three of these studies<sup>3,4,13</sup> reported the administered maintenance anesthetic agent; however, authors did not relate its administration to adverse event occurrence. In our cohort,

Age-at-implantation group	CI < 12 mo.	CI 12-24 mo.	Total (% total no.)	P-value
No. of anesthetic adverse events during 1 CI surgery				.470
0	6	6	12	-
1	5	13	18	-
2	5	6	11	-
3	3	2	5	-
<b>No. of CI surgeries</b>	<b>19</b>	<b>27</b>	<b>46 (100%)</b>	-
Type of anesthetic adverse events (during 1 CI surgery)				
Respiratory event	5	8	13	.538
Gastrointestinal event	8**	9	17	.382
Fever	1	3	4	.448
Excessive pain	1	1	2	.661
Skin reaction	1	1	2	.661
Facial edema	4	6	10	.610
Nosebleeds	4	3	7	.303
<b>Total number of anesthetic adverse events</b>	<b>24</b>	<b>31</b>	<b>55</b>	-
Type of surgical adverse events (<30 d)				.662
Otitis media treated with AB	2	1	3 (6.5%)	-
Vertigo	1	1	2 (4.4%)	-
Meningitis*	0	1	1 (2.2%)	-
<b>Surgical adverse events (total no.)</b>	<b>3</b>	<b>3</b>	<b>6</b>	<b>.484</b>
Type of surgical adverse events (>30 d)				
Otitis media treated with AB	2	2	4 (8.7%)	-
Skin infection treated with AB	0	2	2 (4.4%)	-
CI failure needing intervention	1	1	2 (4.4%)	-
CI infection needing intervention*	2	1	3 (6.5%)	-
<b>Surgical adverse events (total no.)</b>	<b>5</b>	<b>6</b>	<b>11</b>	<b>.508</b>

Note: Respiratory anesthetic adverse events included the following: bronchospasm, inspiratory stridor, and desaturation. Gastrointestinal anesthetic adverse events included the following: nausea and/or vomiting, (n = 16) and diarrhea (n = 1). Two asterisks (\*\*) mark the infant who suffered from diarrhea postoperatively. Major surgical adverse events are marked with one asterisk (\*). Group totals are marked in **bold**.

Abbreviations: AB, antibiotics; CI(s), Cochlear Implant(s); no., number.

infants received sevoflurane more frequently which might be caused by the inhalation induction technique being continued during maintenance at younger age; however, Yeh et al<sup>4</sup> did not identify this relation.

Reported anesthetic adverse event rates during pediatric CI surgery vary between 0%<sup>2,4,13,14</sup> and 8.4%.<sup>3</sup> In line with O'Connell et al,<sup>2</sup> none of our patients suffered from major anesthetic adverse events. However, during 34 CI surgeries, 55 minor anesthetic adverse events

**TABLE 3** All recorded anesthetic and surgical adverse events occurring during 46 included CI surgeries performed in 43 patients, arranged according to age-at-implantation groups

occurred, which is high compared to aforementioned adverse event rates.<sup>2-4,13</sup> This can be explained by selection of three different data sources,<sup>12</sup> a stringent approach that could have resulted in identifying more anesthetic adverse events than previous studies.<sup>2-4,13</sup> Furthermore, reported events could have been considered too minor to report by previous authors. For example, the level of nosebleeds was high in our studied cohort (15.2%), most likely resulting from intraoperative use of a nasal thermometer.

Respiratory events occur more frequently during ear, nose, and throat surgery.<sup>15</sup> These events are even the most frequently reported anesthetic adverse events during pediatric CI surgery (4.7%).<sup>4</sup> Similarly, respiratory adverse events occurred frequently in our cohort (13 out of 46 surgeries: 28.3%).

The incidence of surgical adverse events (13%) in our cohort is relatively high. Previous studies reported surgical adverse event rates ranging between 3.2% to 24.7%.<sup>3</sup> A recent review reported a meningitis occurrence of 0.15% in CI patients (8 out of 5234 patients),<sup>16</sup> indicating that meningitis following CI surgery is rare. The toddler who was suspected of meningitis in our cohort received antibiotic treatment in accordance with studies suggesting aggressive AOM and mastoiditis treatment to reduce meningitis risk.<sup>17,18</sup> Our patient did not undergo a lumbar puncture to confirm diagnosis and could be preventively over-treated, excluding this case results in a 10% surgical adverse event rate.

Since postoperative pain levels are difficult to measure in children, establishing adequate postoperative analgesia seems essential.<sup>3,19</sup> Although one study reported that only 68.8% of the included children needed analgesia following CI surgery,<sup>19</sup> all included patients received postoperative analgesia through paracetamol, and, on indication, diclofenac and/or morphine. The same study showed that analgesics use was distributed similarly among five age-at-implantation groups,<sup>19</sup> which is contrary to our findings in which diclofenac was administered more frequently in toddlers. This finding can be explained twofold: first, according to our local protocol, no diclofenac is administered in infants below 6 months of age, and second, toddlers might have needed additional diclofenac because of the high rate of bilateral CI surgeries in this age group. Children have no pain free side to lie on following bilateral surgery and could therefore need postoperative analgesics for a longer period.<sup>19</sup>

Although minor anesthetic adverse events do not lead to serious long-term complications, they can still result in less comfortable children and (even) more anxious parents, especially when their child is not hospitalized.<sup>4</sup> In our cohort, most patients were hospitalized until 1 day postoperatively, which is in line with previous studies.<sup>12-21</sup> Our results favor this 1-day hospitalization due to both the (a) high rate of minor anesthetic adverse events (74%) and (b) perioperative morphine administration (leading to more gastrointestinal adverse events). Since children can be safely discharged from the PACU when no unexpected postoperative issues arise,<sup>7</sup> implementation of adjusted anesthetic protocols could lead to performing day-case surgery successfully.

Infants have an increased risk of hypoxia and bradycardia during general anaesthesia<sup>22</sup> due to their relative immature sympathetic response<sup>22</sup> and their decreased functional residual lung capacity (which renders them susceptible for hypoxia<sup>2</sup>). Therefore, previous research advocates to perform elective surgery in candidates over 12 months of age.<sup>6</sup> Although (anesthetic) adverse event occurrence seems inversely related to the age at surgery, the benefit of early CIs<sup>1</sup> initiates performing CI surgery soon after birth to prevent speech and language developmental delay.<sup>23</sup> Currently, pediatric CI surgery is performed in relatively older infants, which might lower

the aforementioned infant-related anesthetic risks.<sup>6,24</sup> This is in line with results from our study, in which relatively older infants were included (ie, close to 12 months old). The relative minor age-at-implantation difference between studied groups (0.79 vs 1.19 years) could also explain why no adverse event differences between groups were found.

The generalizability of the present study is limited since one surgeon in a single center performed all surgeries. The present results apply to preoperative anesthesia-related procedures for CI candidacy assessment and CI surgeries under supervision of a pediatric-trained anesthesiologist and performed in healthy infants (ASA 1 or 2), which are factors associated with improved outcome.<sup>3,25</sup> Furthermore, the retrospective nature of the present study with limited sample size limits to draw conclusive recommendations. Lastly, preventive antiemetic administration was not standard practice in the present cohort. New surgical and anesthetic techniques such as local infiltration with long-acting local anesthetics, standard use of nonsteroidal anti-inflammatory drugs (NSAIDs), opioids only on indication and preemptive multimodal prevention and treatment of postoperative nausea and vomiting (PONV) could improve clinical outcome.

The present study shows that both surgical and anesthetic adverse events occurred independently of the age at implantation, the number of preoperative anesthesia-related procedures for CI candidacy assessment and the type of anesthetic maintenance agent in ASA 1 or 2 patients implanted before 24 months of age. Therefore, the optimal pediatric cochlear implantation age could be directed toward infants.

## ETHICAL APPROVAL

The UMCU Institutional Review Board provided ethical approval for this study (protocol number: METC 15-327/C).

## CONFLICT OF INTEREST

None of the authors, besides Dr. JC de Graaff, declares any conflict of interest. Dr. J.C. de Graaff is part of the editorial board of the *Pediatric Anesthesia* journal.

## MEETINGS

This study was presented during three oral presentations:

1. The 14th International Conference on Cochlear Implants and Other Implantable Technologies (CI 2016) in Toronto, Canada (May 11-14, 2016)
2. The 13th European Symposium Pediatric Cochlear Implant (ESPCI) in Lisbon, Portugal (May 25-28, 2017)
3. The 15th International conference on cochlear implants and other implantable auditory technology in Antwerp, Belgium (June 27-30, 2018)

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## SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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