Cardiology in the Young

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Ambulatory sedation for children under 6 years with CHD in MRI and CT

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Original Article

Cite this article: Reichl N, Rabl E, Shehu N, Ferrari I, Martinoff S, Wiesner G, Stern H, Ewert P, and Meierhofer C (2024) Ambulatory sedation for children under 6 years with CHD in MRI and CT. *Cardiology in the Young* **34**: 647–653. doi: 10.1017/S1047951123003207

Received: 25 October 2022
Revised: 12 July 2023
Accepted: 6 August 2023
First published online: 11 September 2023

Keywords:
Sedation; imaging; paediatrics

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Abstract

Introduction: In infants and young children, good image quality in MRI and CT requires sedation or general anesthesia to prevent motion artefacts. This study aims to determine the safety of ambulatory sedation for children with CHD in an outpatient setting as a feasible alternative to in-hospital management. *Methods:* We recorded 91 consecutive MRI and CT examinations of patients with CHD younger than 6 years with ambulatory sedation. CHD diagnoses, vital signs, applied sedatives, and adverse events during or after ambulatory sedation were investigated. *Results:* We analysed 91 patients under 72 months (6 years) of age (median 26.0, range 1–70 months; 36% female). Sixty-eight per cent were classified as ASA IV, 25% as ASA III, and 7% as ASA II (American Society of Anesthesiologists Physical Status Classification). Ambulatory sedation was performed by using midazolam, propofol, and/or S-ketamine. The median sedation time for MRI was 90 minutes (range 35–235 minutes) and 65 minutes for CT (range 40–280 minutes). Two male patients (age 1.5 months, ASA II, and age 17 months, ASA IV) were admitted for in-hospital observation due to unexpected severe airway obstruction. The patients were discharged without sequelae after 1 and 3 days, respectively. All other patients were sent home on the day of examination. *Conclusion:* In infants and young children with CHD, MRI or CT imaging can be performed under sedation in an outpatient setting by a well-experienced team. In-hospital backup should be available for unexpected events.

What's known on this subject

In MRI and CT imaging, patients must lie motionless for long periods of time. For severely ill young patients, general anesthesia is currently the gold standard due to its safety. It often requires, however, in-hospital stays and adds cost.

What this study adds

Ambulatory sedation for imaging in MRI and CT is a feasible alternative to in-hospital management even in children with severe CHD.

CHD is the most common congenital disorder. Its prevalence worldwide is 6.9–9.3/1000, and severe CHD is found in 2.5–3/1.000 live births.[1–3] Long-term survivorship has greatly improved over the recent decades, with up to 97 per cent of children born with CHD reaching adulthood today.[4–6]

Echocardiography, cardiovascular MRI, and CT are the mainstays of non-invasive imaging modalities:[7] Echocardiography is used as a first-line tool for initial diagnosis and follow-up examinations of CHD patients.[8,9] In cases where echocardiography is inconclusive or delivers incomplete imaging, MRI and CT are routinely utilised to confirm the patients' diagnoses, cardiac anatomy, and haemodynamic condition.[10–12] Both techniques record detailed anatomy of the heart and its extracardiac vessels, allowing reliable volume and size calculations of the structures in question. In addition, MRI can capture cine imaging, which provides movie-like information about ventricular and valvular functions. Furthermore, MRI can examine tissue characteristics and cardiac blood flow.[7,13]

On the other hand, CT and especially MRI are time-consuming imaging procedures, thus requiring general anaesthesia or sedation to avoid motion artefacts of the young children during image recording. According to the American Society of Anesthesiologists, sedation can range from minimal sedation with anxiolysis without cardiopulmonary effects (level I) to moderate sedation with preserved respiratory drive (level II), to deep sedation, in which protective reflexes are partially lost (level III). In general anaesthesia (level IV), there is no spontaneous ventilation and intubation is required.[14] Minimal to moderate sedation with preserved spontaneous

breathing was used for this study. This has been established as a viable option for haemodynamically stable children with CHD and avoids the haemodynamic effects of positive pressure ventilation.[15]

Since in children several diagnostic and therapeutic procedures can generally be performed under sedation in an outpatient setting, this study's aim is to test the hypothesis that outpatient sedations for MRI and CT examinations can be performed routinely in the same way for infants and young children with CHD.

Methods

We retrospectively analysed medical records of young children under 6 years of age with CHD who had undergone consecutive ambulatory sedation for MRI and CT. Descriptive statistics such as patient demographics, types of sedatives, vital parameters, overall success, and adverse events are presented. The study was performed in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Patients

The population for this comparative consisted of 91 infants and children (36% female) with CHD under 6 years of age who received ambulatory sedation for cardiovascular MRI or CT from June 2017 to February 2021 as a part of their regular treatments and check-ups. The children's median body weight was 12.0 kg (range 4.1–22.5 kg), and their median age was 26 months (range 1–70 months). The complete age distribution is shown in Figure 1.

The study's patients had heterogeneous diagnoses of CHD, listed in detail in Table 1.

Prior to sedation, the children were classified using the ASA physical status classification system. ASA ratings were available for all patients. Sixty-eight per cent were classified as ASA IV. The ASA distribution is shown in Table 2.[16]

Study procedure – clinical settings

Prior to the regularly scheduled MRI or CT, the patients' health records were reviewed. If a patient was too young to lie motionless for the duration of the procedure, the patients' parents or legal guardians were informed about the planned procedural sedation. Anaesthesia staff contacted them the day before the sedation to obtain consent and instructed them about fasting.

Directly before sedation, the paediatric cardiologists examined the patients to exclude acute cardiorespiratory compromises. Monitoring was performed with continuous electrocardiogram, non-invasive blood pressure measurements, pulse oximetry, and end-tidal carbon dioxide surveillance. All infants were fitted with oxygen masks. Thereafter, anaesthesiologists specialised in paediatric cardiovascular anaesthesia initiated sedation in a room next to the imaging facilities, and the patient was transferred to the MRI or CT scanner while receiving sedatives. The scanning in MRI or CT did not differ to routine in-hospital examinations.

After scanning, sedation was stopped, and the patients awoke in the recovery room under anaesthesiology supervision. They were sent home after an observational period of at least 3 hours and after drinking fluids without problems. Emergency intubation was always available on standby. Before discharge, all parents received a clear briefing for the management of very unlikely late adverse events and were instructed to report the hospital staff immediately in such a case.

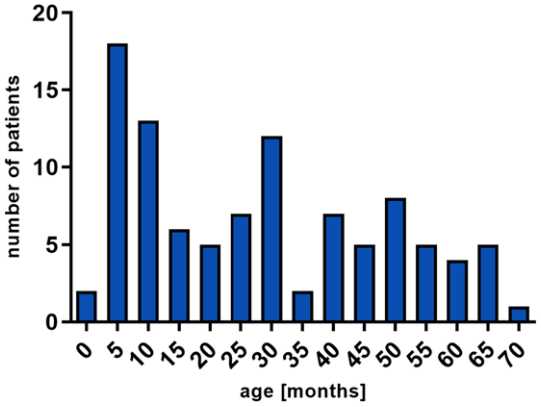

Figure 1. Patients' age distribution.

Analysis and statistics

All records were analysed for overall success defined as good image quality and the absence of lasting adverse events. Adverse events were defined as instability of blood pressure, bradycardia or tachycardia, and persistent impairment of spontaneous respiration.

Descriptive statistics were performed for medication, time of sedation and imaging, and adverse events. The children's heart rate, median arterial pressure, and oxygen saturation during sedation were analysed at four time stamps: at the start of sedation, 10 minutes later, at the end of sedation, and for the last time shortly before the patients' discharge. The values are shown as median and range. These values were tested for significant differences between the recorded time points with analyses of variance (ANOVA) and mixed-effects analyses. The Kolmogorov–Smirnov test was used as nonparametric test. Figures are visualised as boxplot (Tukey), whiskers are maximum 1.5 times of the interquartile range ending at the last data point within this range. All data were processed with Microsoft Excel® 16.52 (Microsoft Corporation, Redmond, WA) and visualised using GraphPad PRISM® 9.2.0 (GraphPad Software, San Diego, CA).

Results

General medication and sedatives

Before being sedated, the children received the imidazole derivate xylometazoline as nasal decongestant if deemed necessary by the anaesthesiologist on duty (n = 27). All patients were supplied with oxygen (median 3.0 (range 1.0–6.0 L/min), its flow depending on their prior saturation, which was median 96 % (range 68 to 100%).

Two children did not receive any of the following intravenous sedation because IV placement was not successful.

Most patients with a weight of less than 10 kg were administered 5 µg/kg atropine intravenously (n = 14). Those with more than 10 kg of body weight received 5 µg/kg the long-acting anticholinergic drug glycopyrronium (n = 57).

Sedatives used for ambulatory sedation were midazolam, propofol, and S-ketamine. All sedatives were applied intravenously except for midazolam, which was also administered intranasally when patients were too agitated for initial intravenous access. Clonidine was used as an add-on to avoid blood pressure spikes and due to its mild sedative properties.

Midazolam was administered initially at 0.1 mg/kg body weight intravenously. S-ketamine was dosed at 0.5 mg/kg. All medications

https://doi.org/10.1017/S1047951123003207 Published online by Cambridge University Press

Table 1. CHD diagnoses of the study population

Diagnosis	n	[%]	n/c/p	Diagnosis	n	[%]	n/c/p
Tetralogy of Fallot	11	12	c	Hypoplastic left heart	1	1	p
Aortic anomaly	8	9	n/c	Pulmonary valve agenesis	1	1	c
Sinus venosus defect	8	9	n	Tricuspid regurgitation	1	1	n
TGA	8	9	c	Ventricular diverticulum	1	1	n
Aortic coarctation	6	7	n/c	Hypertrophic cardiomyopathy	1	1	n
Pulmonary stenosis	5	5	c	ALCAPA	1	1	n
Pulmonary atresia	5	5	c	TCPC	1	1	p
Aortic stenosis	4	4	n/c	Myocarditis	1	1	n
RVOT obstruction	3	3	c	LPA stenosis	1	1	n
Cardiac tumours	3	3	n	Aortopulmonary window	1	1	c
Loeys–Dietz syndrome	3	3	n	Ebstein's anomaly	1	1	n
Kawasaki disease	3	3	n	Scimitar syndrome	1	1	n
Atrial septal defect	3	3	n	Aortic aneurysm	1	1	c
DORV	2	2	n/c	ASD	1	1	n
PCPC	2	2	p	Mitral valve regurgitation	1	1	n
Marfan syndrome	2	2	n				

ASD = atrial septal defect; ALCAPA = anomalous left coronary artery from the pulmonary artery; DORV = double-outlet right ventricle; LPA = left pulmonary artery; n/c/p = native/corrected/palliated condition; PCPC = partial cavo-pulmonary connection; RVOT = right ventricular outflow tract; TCPC = total cavo-pulmonary connection; TGA = transposition of the great arteries. For each diagnosis group, we show the cardiac condition at the time of the ambulatory sedation.

Table 2. ASA physical status classification system

	ASA II	ASA III	ASA IV
n	6	23	62
[%]	7%	25%	68%

ASA classifications according to the American Society of Anesthesiologists (ASA). None were classified as ASA I or V. ASA II includes asymptomatic congenital cardiac disease, ASA III is assigned to children with uncorrected stable congenital cardiac anomalies, and ASA IV refers to symptomatic congenital cardiac abnormalities.[27]

Table 3. Combinations of sedatives used for ambulatory sedation

Sedative	n	[%]
Midazolam, propofol	47	52%
Midazolam, propofol, and S-ketamine	36	42%
Midazolam, propofol, and sevoflurane	2	2%
Midazolam and S-ketamine	2	2%
Midazolam	1	1%
Midazolam, propofol, and fentanyl	1	1%

were titrated to the effective dosage. Continuous propofol was provided with infusion pumps for the duration of the imaging except for four patients (4.7% of propofol recipients) who received single doses. Propofol was started at 10 mg/kg/h to achieve deep sedation. It was then reduced to 4–6 mg/kg/h as maintenance dosage.

Forty-seven patients (52%) received midazolam followed by propofol, while 36 patients (40%) were sedated with midazolam, propofol, and S-ketamine. Two children (2%) were given midazolam followed by S-ketamine. In two cases (2%), sevoflurane was applied instead of S-ketamine for sedation induction. Fentanyl was used in combination with propofol and midazolam in a single instance (1%). One child received only midazolam for sedation (1%). The complete sedative combinations are shown in Table 3. Clonidine was applied as an add-on for 47 sedations (52%). Its use was gradually increased during the second half of the analysed periods, while S-ketamine was less often used.

During sedation, 76 children (84%; body weight < 20 kg) received an electrolyte/glucose infusion, and 15 patients (16%; body weight ≥ 20 kg) Ringer's solution.

Duration of sedation and imaging

The median time spent asleep for MRI (73 patients) and CT (14 patients) was 90 min (range 35–235 min) and 65 min (40–280 min), respectively ($p = 0.053$; $n = 87$; four single missing time points in four reports). The core scan time for MRI and CT was 50 min (range 5–205 min) and 20 min (range 10–35 min), respectively. As expected, the scan time difference was statistically significant ($p < 0.0237$). The data are depicted in Figure 2.

Image quality

Almost all examinations resulted in satisfactory image quality. Inadequate sequences were repeated immediately if the schedule and child's condition allowed it. One MRI examination had to be redone because an adverse event forced the staff to stop the scan but not due to insufficient image quality. It was completed on the following day using cardiac CT. The quality of the acquired images was not systematically rated by the staff.

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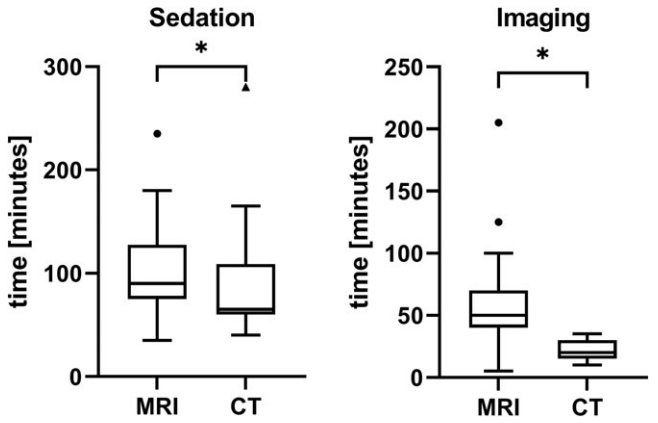

Figure 2. Duration of complete sedation time and imaging time for MRI and CT. Boxplot (Tukey) of the sedation times for complete sedation period and times for imaging only.

Vital signs

As shown in Figure 3, arterial blood pressure decreased significantly during sedation. Initially, the heart rate was stable for the first 10 minutes but decreased significantly over the course of the sedation. Conversely, the patients' oxygen saturation increased significantly due to the supplied oxygen from median 96% (68–100%) to median 99% (86–100%). Since patients were not intubated, $etCO_2$ was used for qualitative assessment of the respiration.

Comparing the patients who received MRI with those who received CT, the course of the monitored vital parameters did not yield any pronounced differences, except for the oxygen saturation: The children who were examined in MRI had slightly higher oxygen saturations at the start of sedation, after 10 minutes, and at discharge.

Adverse events

Three adverse events were observed over the course of 91 examinations (event rate 3.3%). A patient (age 1.5 months, male; ASA II) with a suspected double aortic arch anomaly had to be evaluated by cardiac MRI. He was in good condition before the induction of sedation using midazolam and propofol but experienced airway obstruction caused by increasing bronchial secretion after a total of 120 minutes in sedation. After receiving atropine, epinephrine, short-acting glucocorticoids, and manual ventilation, but no intubation, he was admitted for in-hospital observation but required no additional treatment. Image quality was satisfactory, and the patient was discharged on the next day without sequelae. Aortic arch anatomy was ruled out to be culprit of the adverse event, since respiratory problems started first after a long sedation time.

Another patient (age 17 months, male; ASA IV) with cleft palate, trisomy 21, tetralogy of Fallot after corrective surgery a year before and two pulmonary hypertensive crises in his medical records, developed severe bronchial secretion and spasms resulting in insufficient spontaneous breathing 30 min after sedation with midazolam and propofol for an MRI scan. He experienced hypotension and bradycardia, needed manual bagging and chest compression for 30 seconds as well as drug-based resuscitation. He immediately recovered and was admitted for in-hospital observation. Cardiac imaging was completed the following day without sedation using a CT scan. The patient was discharged 3 days after without sequelae.

Another patient (age 7 months, male; ASA IV) with corrected transposition of the great vessels received atropine due to bradycardia during his MRI scan. The recorded heart rate did not decrease under 70 bpm, and the scan was completed successfully.

All other patients were sent home after a minimum observational period of 3 hours on the day of their ambulatory sedation.

Discussion

For MRI and CT, lying motionless is necessary to obtain good image quality. Non-pharmacological calming methods are a viable option but can be ineffective in infants and young children.[17,18] This is of major importance for CT scans because the risk of repeated radiation exposure due to failed imaging acquisition must be minimised especially in children.[19,20]

As a result, general anaesthesia has been established as the gold standard for these patient groups because it offers a high level of procedural success and safety through airway management. However, general anaesthesia also has disadvantages. Intubation can affect the patient's haemodynamics and therefore the accuracy of cardiac diagnosis. In cases where post-operative overnight observation is planned, it may require increased hospital resources and cause organisational effort and expense for the hospital and the patient's family.[21–24]

In this context, this study demonstrates an alternative for children with CHD under the age of 6 years. They can be sedated safely for MRI and CT in an ambulatory setting, even at a very young age and ASA class IV.

Our findings go beyond the results of other groups such as Rangamani et al and Fogel et al, which used different medications and were mostly limited to sedations in conventional inpatient treatment or had different patient cohorts, respectively.[15,25]

For this study, arterial pressure, heart rate, and oxygen saturation were analysed at four specific time points (Fig 3). The statistical differences in between those values were attributable to the sedation effect on the children's impaired cardiovascular systems. The patients' oxygen saturation, which was supported through external oxygen supplementation during sedation, reached pre-sedation levels at the time of discharge. Hence, in patients with cyanotic and acyanotic CHD, external oxygen supply generally serves as an additional safety component for sedation. It has also to be considered, that in patients with cyanotic CHD too much pulmonary flow due to increased oxygen supply may deteriorate the patients' condition and haemodynamics and must be well balanced by an experienced team.

This study reported a 3.3% rate of adverse events and is comparable to that of Fogel et al. He reported a rate of 2.8% of self-limiting adverse events in patients with a mean age of 51.6 months,[15] while our group was younger with a mean age of 28.3 months (median 26 months).

It is, however, very important to understand that the reason for the adverse events had clearly been due to the patients' cardiovascular conditions and not due to the ambulatory setting. Almost 70% of our study patients were in ASA group IV, documenting that more than 2/3 of the patients suffered from severe cardiovascular disease. Therefore, the described adverse

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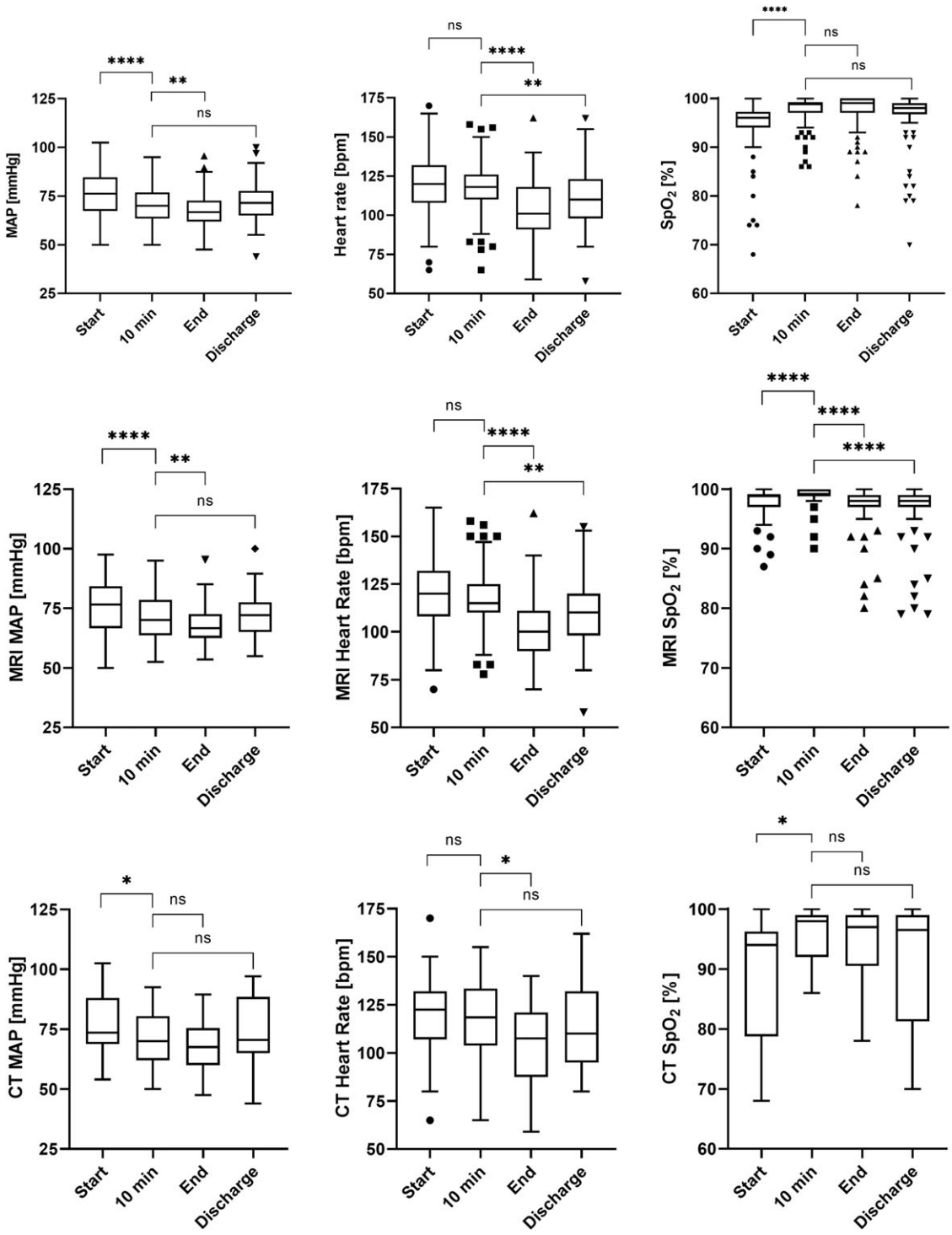

Figure 3. Vital signs before, during, and after sedation. Boxplot (Tukey) at four time points during ambulatory sedation. Arterial pressure, heart rate, and oxygen saturation are shown. Time point 1 displays the start of the sedation and time point 2 records at 10 minutes after the start of sedation. Time point 3 at the end of sedation, time point 4 at the last recorded vital signs at discharge from sedation surveillance. Upper row: all patients (n = 91); middle row: patients with MRI scans (n = 76); lower row: patients with CT scans (n = 15).

events may probably have occurred in an in-hospital setting in a similar way. Thus, the questions, which must be addressed, is, whether the incidences had been medically handled differently if the patients had come from an in-house ward instead from home? We are convinced that in our tertiary centre specialised for the treatment of patients with CHDs, there would have been no differences in the handling, which is underlined by the uneventful recovery of both patients.

To prevent adverse events, essential additional cornerstones are the consulting of the referring physician, the review of past records, the interview of the patients' parents beforehand, and the physical examination of the patients immediately prior to sedation.

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Since unexpected events cannot be completely ruled out during sedation of young children with CHD, facilities for all necessary emergency procedures must be easily available at any time. Therefore, sedations at our centre were carried out only by staff trained in paediatric advanced life support with extensive experience in cardiac anaesthesiology. Critical care teams and surgical teams were available at a moment's notice in the same building. Krauss et al. reported similar recommendations.[26] Almost all of our tertiary centre patients are in our long-term care including outpatient visits and invasive in-house procedures like open-heart surgery and transcatheter interventions. Thus, most of their health records are complete and available at our centre.

Our study is limited by its retrospective design. It was not intended to investigate different drug regimens for ambulatory sedation nor to compare the data with in-house-treated groups. However, it proves the feasibility of the procedures. In the meantime, all MRI/CT scans of pre-school children and of infants with CHDs are currently performed under ambulatory sedation.

These children, who had often experienced several hospital stays for surgery and cardiac recovery, can benefit from CT or MRI scans and still can quickly return to their home, saving parents' time and nerves and hospital costs at the same time.

Conclusion

In infants and children with CHD, MRI and CT scans can be routinely performed in an outpatient setting at a tertiary heart centre even if the patients have considerable cardio-circulatory risk factors according to the ASA classification.

Acknowledgements. We thank the German Heart Centre Munich anesthesiology nursing staff for their excellent work. This study was not supported by external sources.

Author contribution. Nicolas Reichl designed the study, collected data, performed the statistical analysis, drafted the manuscript, and reviewed and revised the manuscript.

Elisabeth Rabl was responsible for the coordination and supervision of sedation, data collection and reviewed and revised the manuscript.

Nerejda Shehu, Irene Ferrari, and Heiko Stern collected data, reviewed, and revised the manuscript.

Gunther Wiesner, Peter Ewert, and Stefan Martinoff critically reviewed the manuscript.

Christian Meierhofer conceptualised and designed the study, performed the statistical analysis, drafted reviewed, and revised the manuscript.

All authors approved the final manuscript and agree to be accountable for all aspects of the work.

Financial support. This research received no specific grant from any funding agency, commercial, or not-for-profit sectors.

Competing interests. None.

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