PICU Autopsies: Rates, Patient Characteristics, and the Role of the Medical Examiner

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Objectives: Autopsy rates in North American Children's hospitals have not been recently evaluated. Our objectives were 1) to determine the autopsy rates from patients cared for in PICUs during a portion of their hospital stay, 2) to identify patient characteristics associated with autopsies, and 3) to understand the relative role of medical examiner cases.

Design: Secondary analysis of data prospectively collected from a sample of patients (n = 10,078) admitted to PICUs affiliated with the Collaborative Pediatric Critical Care Research Network between December 2011 and April 2013.

Setting: Eight quaternary care PICUs.

Patients: Patients in the primary study were less than 18 years old, admitted to a PICU and not moribund on PICU admission. Patients included in this analysis were those who died during their hospital stay.

Interventions: None.

Measurements and Main Results: Sociodemographic, clinical, hospital, and PICU data were compared between patients who had autopsies conducted and those who did not and between medical examiner and nonmedical examiner autopsies. Of 10,078 patients, 275 died of which 36% (n = 100) had an autopsy performed. Patients with cancer who died were less likely to receive autopsies ($p = 0.005$), whereas those who died after trauma or cardiac arrest had autopsies performed more often ($p < 0.01$). Autopsies were more common in patients with greater physiologic instability at admission ($p < 0.001$), and those who received more aggressive PICU care. Medical examiner cases comprised nearly half of all autopsies ($n = 47$; 47%) were conducted in patients presenting with greater physiologic instability ($p < 0.001$) and more commonly after catastrophic events such as cardiac arrest or trauma ($p < 0.001$).

Conclusions: In this first multicenter analysis of autopsy rates in children, 36% of deaths had autopsies conducted, of which nearly half were conducted by the medical examiner. Deaths with autopsy are more likely to be previously healthy children that had catastrophic events prior to admission. (*Pediatr Crit Care Med* 2018; XX:00–00)

Key Words: autopsy; death; medical examiner; pediatric intensive care unit

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Autopsy rates in adults have steadily declined in the last half century from nearly 50% to less than 20% (1–4). This decline has been attributed to advances in

diagnostic and imaging techniques that make autopsies less informative, difficulties obtaining consent, and loss of interest by clinicians (3). Approximately 25% of autopsies on adults resulted in a diagnosis that was missed clinically and for up to 10% of cases, the new diagnosis would have resulted in a change in clinical care that may have led to recovery or prolonged survival if it had been known before death (3, 5). In the past, physicians believed that autopsies provide valuable information, should be performed more frequently, and may provide support for grieving families (6).

The most recent North American pediatric autopsy rates from the 1990's range between 26% and 40% in single-center studies (2, 7, 8). None of the previous reports focused on identifying patient characteristics associated with autopsies. Similar to adult results, single-center pediatric studies found discordance between the premorbid and autopsy diagnostic information in 16–30% of cases (8–10).

Most pediatric deaths occur either in the PICU or involve patients who had care delivered in the PICU for part of their hospitalization (11). The objectives of this project were to determine the autopsy rate among patients cared for in the PICU, to identify patient characteristics associated with autopsies, and to understand the current role of medical examiner cases in performing autopsies.

METHODS

This study was a secondary analysis of data collected prospectively in a 10,078 patient probability sample of all patients admitted to PICUs in the eight sites in the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development Collaborative Pediatric Critical Care Research Network between December 2011 and April 2013 (12). Patients in this sample were less than 18 years old and admitted to a medical/surgical or cardiac PICU. Patients were excluded in the primary data set if their vital signs were incompatible with life for at least the first 2 hours after PICU admission. Data were collected at the time of first PICU admission for each of the 10,078 patients. The protocol was approved by the Institutional Review Boards at all participating institutions. This analysis focuses on PICU patients who died during their hospitalization, including children who died during the initial PICU stay, whereas readmitted to the PICU, or elsewhere in hospital.

Data Collection

Details of data collection have been previously reported (12, 13). Sociodemographic data included sex, age, race, ethnicity, and payer type. Clinical variables at admission included baseline functional status, underlying conditions (congenital heart disease, acute or chronic cancer), events prior to admission (trauma, cardiac arrest), admission status (elective or emergent), admission source (post operative, inpatient, referral hospital, or emergency department), and primary system of dysfunction at admission (classified as respiratory, cardiovascular [acquired or congenital], cancer, neurologic, or other). Severity of illness was assessed with Pediatric Risk of Mortality (PRISM) scores using laboratory information obtained between 2 hours prior to through 4 hours after PICU admission and vital signs recorded in the first 4 hours post admission. The PRISM score is a physiology-based score for mortality risk (14, 15).

Functional status at admission (baseline) was assessed with the Functional Status Scale (FSS) using historical information at hospital admission. The FSS is a granular scale for assessing pediatric functional status in six domains including mental, sensory, communication, motor function, feeding, and respiratory status (16). Total FSS scores range from 6 to 30 and are categorized as 6–8 (normal and mild dysfunction), 9–13 (moderate dysfunction), 14–20 (severe dysfunction), and greater than 20 (very severe dysfunction).

Autopsies were categorized as medical examiner autopsy only if they were performed by the medical examiner. If the death was referred to the medical examiner, but autopsy was performed in the tertiary children's hospital, it was categorized as a nonmedical examiner autopsy. PICU and hospital resource use included PICU and hospital length of stay. Mechanical ventilation and/or vasoactive agent infusion were used as indicators of aggressive PICU care while antibiotics and/or steroid administrations were used as indicators of nonaggressive PICU care. Variables related to end-of-life care included the date, time, and location of death; whether the death was a medical examiner case; and whether an autopsy was performed. Location of death was categorized as PICU, general care area, or other hospital location.

Statistical Analysis

Statistical analysis was under the supervision of Dr. Holubkov. Binary and categorical data were expressed as absolute numbers and percentages. Continuous data were summarized by medians and interquartile ranges (25–75th percentiles). Statistical analysis used the Wilcoxon rank-sum test to compare continuous factors between subgroups, whereas chi-square tests or Fisher exact tests were used to compare proportions of binary or categorical factors between subgroups. All tests were two-tailed and a probability value less than 0.05 was treated as significant in this exploratory analysis. Statistical analysis was performed in SAS Version 9.4 (SAS Institute, Cary, NC).

RESULTS

Of the 10,078 patients in the cohort, a total of 275 (2.7%) died during their hospital stay, of whom 100 (36.4%) received an autopsy. Autopsy rates were different by study site (**Fig. 1**) ($p = 0.009$ for chi-square comparison of autopsy rates by sites; also $p < 0.001$ for chi-square comparison of medical examiner autopsy rates by site). Sociodemographic and baseline characteristics of the patient deaths with and without autopsy are contained in **Table 1**. Over half the patients ($n = 142$; 51.6%) were male, and 44.4% were less than 1 year old. Although there was no difference in median age between those who were autopsied and those who were not, autopsy rates were lower in some age categories, such as infants under 14 days old and children over 144 months old. The majority of patients (67%) had government insurance; payer type was not associated

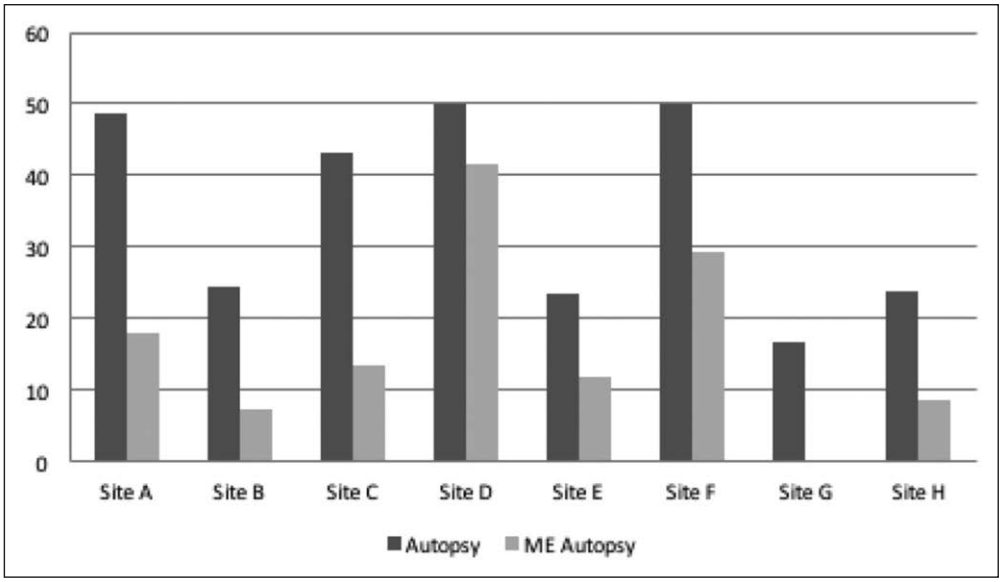

Figure 1. Proportion of deaths that were autopsies and medical examiner (ME) autopsies by site.

with autopsy rate. Race and ethnicity were not assessed in this report due to a large number of missing values.

Admission characteristics of patient deaths with and without autopsies are depicted in **Table 2**. Baseline functional status, whereas normal, was worse in children without autopsies than those with autopsies, as seen by the larger interquartile range for nonautopsied children (p = 0.046). Congenital heart disease was not significantly associated with autopsies. However, children who died with an underlying condition of cancer were less likely to have an autopsy conducted (p = 0.005). Patients who presented to the ICU after trauma or after cardiac arrest were significantly more likely to have an autopsy than others. Elective versus emergent admission status, admission source, and primary system of dysfunction at admission to the PICU were not significantly associated with autopsy status.

Patients with autopsies had shorter, but more aggressively treated illnesses than patients without autopsies (**Tables 2** and **3**). Patients with autopsies had worse severity of illness (median PRISM scores: 18 vs 11; $p < 0.001$), and a shorter length of stay in the PICU (median, 3.2 vs 6.2 d; $p = 0.04$) as well as shorter hospital stay (median, 4.9 vs 13.5 d; $p = 0.001$). PICU therapies including mechanical

TABLE 1. Sociodemographic Characteristics of Deaths by Autopsy Performance

Variables	Deaths With Autopsy, $n = 100$	Deaths Without Autopsy, $n = 175$	Significance Level
Gender, *n* (%)			0.73[a]
Male	53 (37.3)	89 (62.7)	
Female	47 (35.3)	86 (64.7)	
Age, median (interquartile range)	0.9 (0.3–7.2)	2.0 (0.2–9.8)	0.26[b]
Age category, *n* (%)			< 0.001[a]
0 to < 14 d	13 (26.5)	36 (73.5)	
14 d to < 1 mo	2 (40.0)	3 (60.0)	
1 to < 12 mo	36 (52.9)	32 (47.1)	
12 to < 60 mo	18 (29.5)	43 (70.5)	
60 to < 144 mo	22 (51.2)	21 (48.8)	
≥ 144 mo	9 (18.4)	40 (81.6)	
Payer type, *n* (%)			0.88[a,c]
Government	67 (36.6)	116 (63.4)	
Commercial	24 (33.3)	48 (66.7)	
Other	3 (37.5)	5 (62.5)	
Unknown	6 (50.0)	6 (50.0)	

[a]Chi-square test.
[b]Wilcoxon rank-sum test.
[c]Excluding unknowns.

TABLE 2. Autopsy Performance by Clinical Characteristics of Children Who Died

Variables	Autopsy, *n* = 100	No Autopsy, *n* = 175	Significance Level
Baseline function, median (IQR)			
Baseline Functional Status Scale	6 (6–8)	6 (6–10)	0.046[a]
Underlying conditions, *n* (%)			
Cancer diagnosis			0.005[b]
Present	5 (14.7)	29 (85.3)	
Absent	95 (39.4)	146 (60.6)	
Congenital heart disease			0.13[b]
Present	33 (30.8)	74 (69.2)	
Absent	67 (39.9)	101 (60.1)	
Events prior to admission, *n* (%)			
Trauma			0.006[b]
Yes	14 (63.6)	8 (36.4)	
No	86 (34.0)	167 (66.0)	
Cardiac arrest			< 0.001[b]
Yes	34 (68.0)	16 (32.0)	
No	66 (29.3)	159 (70.7)	
Admission status, *n* (%)			
Elective (scheduled)	17 (34.7)	32 (65.3)	0.79[b]
Emergent (unscheduled)	83 (36.7)	143 (63.3)	
Admission source, *n* (%)			0.82[b]
Postoperative	21 (36.2)	37 (63.8)	
Inpatient	21 (32.8)	43 (67.2)	
Direct admission from referral hospital	36 (40.0)	54 (60.0)	
Emergency department	22 (34.9)	41 (65.1)	
Primary system of dysfunction, *n* (%)			0.35[c]
Respiratory	22 (27.8)	57 (72.2)	
Cardiovascular	49 (38.9)	77 (61.1)	
Cancer	2 (22.2)	7 (77.8)	
Neurologic	18 (43.9)	23 (56.1)	
Gastrointestinal	4 (40.0)	6 (60.0)	
Other	5 (50.0)	5 (50.0)	
Severity of illness, median (IQR)			
Pediatric Risk of Mortality score	18 (7–27)	11 (5–19)	< 0.001[a]

IQR = interquartile range.
[a]Wilcoxon rank-sum test.
[b]Chi-square test.
[c]Fisher exact test.

ventilation and vasoactive infusions were used significantly more often in patients with autopsies ($p < 0.01$), whereas less aggressive therapies such as antibiotics and steroids were not. The majority of patients died in the PICU; there was no difference in the proportion of autopsies based on hospital location of death.

TABLE 3. PICU and Hospital Resource Use by Autopsy Performance

Variables	Autopsy, *n* = 100	No Autopsy, *n* = 175	Significance Level
PICU LOS, d, median (IQR)	3.2 (1.3–13.2)	6.2 (1.8–15.0)	0.04[a]
Hospital LOS, d, median (IQR)	4.9 (1.6–18.1)	13.5 (3.5–31.3)	0.001[a]
Therapies, *n* (%)			
Mechanical ventilation	95 (95.0)	147 (84.0)	0.007[b]
Vasoactive agent infusions	88 (88.0)	124 (70.9)	0.001[b]
Antibiotics	86 (86.0)	152 (86.9)	0.84[b]
Steroids	48 (48.0)	95 (54.3)	0.32[b]
Location of death, *n* (%)			0.31[c]
PICU	95 (95.0)	157 (89.7)	
Hospital general care	2 (2.0)	10 (5.7)	
Other	3 (3.0)	8 (4.6)	

IQR = interquartile range, LOS = length of stay.
[a]Wilcoxon rank-sum test.
[b]Chi-square test.
[c]Fisher exact test.

There were 62 deaths designated as medical examiner cases, of which 76% were autopsied by the medical examiner. Of the 100 autopsies, 47 were conducted by the medical examiner (**Table 4**). There were no significant differences in median age or payer type between medical examiner and the nonmedical examiner autopsies; however, no infants less than 14 days old were medical examiner autopsies. Children who had medical examiner autopsies were more likely to have normal baseline functional status. All autopsied patients who had trauma and the majority of patients with cardiac arrests (85.3%) had them performed by the medical examiner. Among autopsied children, those admitted to the ICU from an inpatient location or operative procedure were less likely to have medical examiner autopsies than those with unscheduled admissions or from the emergency department or referral hospital. The primary system of dysfunction at admission was different between medical examiner autopsies and nonmedical examiner autopsies, with 89% of autopsied children admitted with neurologic dysfunction having medical examiner autopsies, compared with less than half with other dysfunction types. Medical examiner cases had more physiologic instability than other autopsied children (median PRISM scores: 23 vs 11; $p < 0.001$), and had shorter median hospital length of stay (2.8 vs 8.2 d; $p = 0.003$). The intensive care therapies of mechanical ventilation and vasoactive agent infusions were similar between the two groups, whereas nonmedical examiner cases received significantly more (less aggressive) therapies of antibiotics and steroids ($p < 0.05$).

DISCUSSION

This is the largest and only multicenter contemporary analysis of autopsy rates in pediatric patients. The autopsy rate in this study was 36%, similar to other published data from single-center North American pediatric studies (26–40%) (2, 7, 8) and lower than international single-center pediatric studies with rates of 40–60% (9, 17, 18).

A number of observations may be drawn from this analysis. First, patient deaths receiving autopsies are more likely to have had severe, acute conditions. Patient deaths receiving autopsies were more likely to have trauma and cardiac arrests prior to PICU admission, present with greater physiologic instability, and more frequently received aggressive PICU care than those who did not have autopsies. These children had shorter lengths of stay and may have had more limited antemortem diagnostic efforts. Patients not receiving autopsies were more likely to have conditions where the diagnosis was known and more likely to have been comprehensively investigated, such as cancer or congenital heart disease.

Second, medical examiner autopsies comprise about half of all autopsies. This remains consistent with data from over 2 decades ago by Goldstein et al (19), who report a single-center rate of 44% in the PICU. Medical examiner patients predominantly had traumatic injury and/or cardiac arrest. Requirements to refer deaths to medical examiners are dependent on jurisdiction; it was out of the scope of this study to examine these local requirements of each institution. However, to gain better understanding of this, we surveyed each of the sites for autopsy practices. We found only one of seven sites (14%) have mandated referrals of all deaths to the medical examiners. The remainder of cases are referred based on a set of clinical and historical guidelines, which includes suspicious circumstance or evidence of trauma (100%), operative or postoperative death (66.7%), and time from admission to death (83.3%). It is also unclear whether families would have elected to have an autopsy performed if their child was not mandated to have one conducted by the medical examiner. We also analyzed children as medical examiner autopsies only if

TABLE 4. Comparison of Medical Examiner and Nonmedical Examiner Autopsies

Variables	Medical Examiner Autopsies, *n* = 47	Nonmedical Examiner Autopsies, *n* = 53	Significance Level
Sociodemographics			
Gender, *n* (%)			0.66[a]
Male	26 (49.1)	27 (50.9)	
Female	21 (44.7)	26 (55.3)	
Age, median (IQR)	1.1 (0.3–8.6)	0.8 (0.0–5.9)	0.17[b]
Age category, *n* (%)			0.003[c]
0 to < 14 d	0 (0.0)	13 (100.0)	
14 d to < 1 mo	1 (50.0)	1 (50.0)	
1 to < 12 mo	20 (55.6)	16 (44.4)	
12 to < 60 mo	11 (61.1)	7 (38.9)	
60 to < 144 mo	10 (45.5)	12 (54.5)	
> 144 mo	5 (55.6)	4 (44.4)	
Payer type, *n* (%)			0.12[c,d]
Government	29 (43.3)	38 (56.7)	
Commercial	13 (54.2)	11 (45.8)	
Other	3 (100.0)	0 (0.0)	
Missing	2 (33.3)	4 (66.7)	
Baseline function, median (IQR)			
Baseline Functional Status Scale	6 (6–6)	6 (6–9)	< 0.001[b]
Underlying conditions, *n* (%)			
Cancer diagnosis			0.37[c]
Present	1 (20.0)	4 (80.0)	
Absent	46 (48.4)	49 (51.6)	
Congenital heart disease			< 0.001[a]
Present	2 (6.1)	31 (93.9)	
Absent	45 (67.2)	22 (32.8)	
Events prior to admission, *n* (%)			
Trauma			< 0.001[a]
Yes	14 (100.0)	0 (0.0)	
No	33 (38.4)	53 (61.6)	
Cardiac arrest			< 0.001[a]
Yes	29 (85.3)	5 (14.7)	
No	18 (27.3)	48 (72.7)	
Admission status, *n* (%)			
Elective (scheduled)	4 (23.5)	13 (76.5)	0.033[a]
Emergent (unscheduled)	43 (51.8)	40 (48.2)	

(*Continued*)

TABLE 4. (*Continued*). Comparison of Medical Examiner and Nonmedical Examiner Autopsies

Variables	Medical Examiner Autopsies, *n* = 47	Nonmedical Examiner Autopsies, *n* = 53	Significance Level
Admission source, *n* (%)			0.005[a]
Postoperative	6 (28.6)	15 (71.4)	
Inpatient	5 (23.8)	16 (76.2)	
Direct admission from referral hospital	22 (61.1)	14 (38.9)	
Emergency department	14 (63.6)	8 (36.4)	
Primary system of dysfunction, *n* (%)			< 0.001[c]
Respiratory	8 (36.4)	14 (63.6)	
Cardiovascular	22 (44.9)	27 (55.1)	
Cancer	0 (0.0)	2 (100.0)	
Neurologic	16 (88.9)	2 (11.1)	
Other	1 (11.1)	8 (88.9)	
Severity of illness, median (IQR)			
Pediatric Risk of Mortality score	23 (17–31)	11 (5–19)	< 0.001[b]
Resource use			
PICU LOS, median (IQR)	2.8 (1.1–6.3)	4.2 (1.4–22.0)	0.11[b]
Hospital LOS, median (IQR)	2.8 (1.1–6.8)	8.2 (2.4–42.0)	0.003[b]
ICU therapies, *n* (%)			
Mechanical ventilation	46 (97.9)	49 (92.5)	0.37[c]
Vasoactive agent infusions	40 (85.1)	48 (90.6)	0.40[a]
Antibiotics	37 (78.7)	49 (92.5)	0.048[a]
Steroids	16 (34.0)	32 (60.4)	0.009[a]
Location of death, *n* (%)			0.25[c]
PICU	46 (97.9)	49 (92.5)	
Hospital general care	1 (2.1)	1 (1.9)	
Other	0 (0.0)	3 (5.7)	

IQR = interquartile range, LOS = length of stay.
[a]Chi-square test.
[b]Wilcoxon rank-sum test.
[c]Fisher exact test.
[d]Missing variables excluded (two patients with medical examiner [ME] autopsies and four patients with non-ME autopsies).

their autopsy was conducted by the medical examiner. There were 62 medical examiner referrals, of which 15 (24%) were not conducted by the medical examiner. Although not known in our cohort, reasons for this may include the medical examiner denying the referral, lack of expertise of the medical examiner to conduct the autopsy, or instances of organ donation where the medical examiner is present to observe the organ procurement but does not conduct an autopsy.

Most sociodemographic characteristics associated with autopsies in this analysis were similar to previous studies (8, 20). Kumar et al (8) examined sociodemographic factors including age, race, and insurance status and found no difference in autopsy status based on these variables. However, their study found that autopsies were more common in patients over 5 years while our study found a higher rate of autopsies in those 1 month to 1 year old and a lower rate in adolescents. The current study is the first to assess the baseline functional status of children receiving autopsies finding that those receiving autopsies had normal or near-normal baseline functional status.

Although this study is characterized by many strengths including the use of robust data collected initially to assess the relationship of physiologic status to morbidity and mortality, there are also limitations. For example, the dataset excluded patients who had vital signs incompatible with life within the first few hours of admission. These children likely presented

after a sudden event, but their autopsy rate and their characteristics at PICU admission are unknown. Additionally, the pathologic results of the autopsies were not abstracted, and thus, there could be no attempt to correlate these results with clinical diagnoses. Although this information is central to the need for autopsies, it is better collected prospectively with reliable assessments of clinical care, the knowledge of the care givers, and the potential clinical impact of the pathologic results. Survey of our sites did show four of seven sites (57.1%) had a systematic way in which autopsy results were reviewed, yet only two of seven (28.6%) had a similar systematic review of medical examiner case results. Finally, although our intention was to look at "overall" trends in PICUs, our cohort showed institutional heterogeneity among study sites in autopsy rates (~16% to 50%) and in the percentage of medical examiner cases (0 to ~42%). This might reflect the different demographic characteristics of each institution.

CONCLUSIONS

This is the first multicenter pediatric study of autopsy rates in children. Approximately one-third of PICU patients who die have an autopsy conducted, of which half are conducted by the medical examiner. Autopsies are more likely to be performed on previously healthy children with no preexisting medical conditions and normal functional status that incur severe, acute events prior to admission. The autopsy rates in this contemporary study are consistent with other single-center pediatric studies in the United States from prior decades.

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