What New Information Pediatric Autopsies Can Provide

A Retrospective Evaluation of 100 Consecutive Autopsies Using Family-Centered Criteria

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Objective: To determine the proportions of pediatric autopsies yielding various types of new information (eg, genetic diagnosis, additional explanation) that might be valued by families.

Design: Retrospective case series analysis.

Setting: Large urban children’s hospital.


Intervention: Using both traditional criteria and a novel classification scheme developed with expert clinicians and nonmedical parent faculty, 3 reviewers independently assessed each case for new information found at autopsy. Classifications were based on unanimous consensus.

Main Outcome Measure: Proportions of autopsies yielding new information.

Results: Decedents’ ages ranged from 1 to 24 years. Using traditional criteria, major unexpected findings related to death occurred in 28% of the autopsies. Applying our novel criteria to the same 100 autopsies, we found new information that had the potential to further clarify the cause(s) of a child’s death (53% of cases); inform the future reproductive choices of either the parents (10%) or siblings (8%); affect siblings’ future health care (6%); or contribute to patient care quality control (36%) or publishable knowledge (7%).

Conclusions: Pediatric autopsies can yield different types of information that may be important to families. While the proportion of autopsies providing specific types of new information will vary between hospitals (depending on case mix, autopsy policies, and clinician/pathologist expertise) and across time (depending on available diagnostic modalities), hospital-specific data classified in this manner may be useful to physicians counseling families about autopsy.

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WHAT DO THE FAMILIES OF DECEASED CHILDREN DEEM IMPORTANT WHEN CONSIDERING WHETHER TO PURSUE PEDIATRIC AUTOPSY? The broad spectrum of answers offered by the parents of deceased children reinforces the intimately subjective nature of this question.1-3 Parents may request autopsy based on the notion that autopsy will routinely advance medical knowledge, benefit other patients with the same disease, reveal an exact cause of death, or provide reassurance that nothing more could have been done medically.1-3 Alternatively, parents may decline autopsy based on the notions that the deceased patient has already suffered enough, autopsy will significantly disfigure the body, or the decision about autopsy too stressful a choice to make in the immediate postmortem period.1,3

Currently, the decision to obtain or forgo autopsy is hampered by the lack of quantitative, family-centered information that could guide parents regarding the probability that a pediatric autopsy would yield different forms of potentially beneficial information. Instead, studies of pediatric autopsies have focused more narrowly on the accuracy of premortem diagnoses. Current literature suggests that pediatric autopsies are performed in approximately 27% to 67% of childhood deaths,4-8 with new diagnoses or additional medical information discovered in 21% to 76% of autopsy cases9-11 and with significant differences in premortem and postmortem diagnoses in 6% to 39% of patients.5-8,10,12,13 With this emphasis on di-
studies, the value of autopsy is classified using a stan-
digm of how autopsy programs should be evaluated and
viding both families and clinicians with empirical data about
altering patient management.6
sies in clarifying or confirming diagnoses, examining treat-
ment effects, providing quality assurance information, or
ating patient management.6
While such classification schemes provide important
quality feedback for hospitals, the priorities of the par-
ents of dying children may be different from those of phy-
sicians and hospitals.1,3 When counseling parents at the
sidebed about the risks and benefits of pediatric aut-
opsey, physicians may find it difficult to translate tradi-
tionally classified autopsy data into meaningful informa-
tion that addresses parental concerns.14-16 To our
knowledge, in the era of patient- and family-centered care,
no studies have evaluated the new information yielded by pediatric autopsy using criteria that explicitly aim to classify autopsy findings in terms of their potential pertinence to the parents and siblings of dying children. Accordingly, we designed a study that would provide both families and clinicians with empirical data about types of information that may or may not be discovered by a pediatric autopsy. To do so, we expanded the paradigm of how autopsy programs should be evaluated and conducted a retrospective case series analysis to investigate the new information gained from autopsy using a family-centered perspective (Table 2) as well as the traditional classification scheme.

We conducted a retrospective case series analysis of 100 con-
secutive pediatric autopsy cases performed at the Children’s Hos-
pital of Philadelphia between 2003 and 2004. All autopsies were
included in the analysis, including children who had died prior
to arrival at the hospital. The Committees for the Protection
of Human Subjects approved the conduct of this study.

METHODS

We first conducted a structured PubMed review of pediatric
and adult literature using various combinations of relevant MeSH
terms (pediatrics, adult, autopsy, value, family) and their syn-
onyms. Using the findings of published studies,1-5,17,18 we iden-
tified types of information that might be of potential impor-
tance to the families of dying children; the results served as the
basis for the categories of new information (Table 2). Next, to
confirm the scope and appropriateness of the categories, we
presented the classes of new information to an expert panel of pe-
diatric clinicians (including physicians from neonatology, pe-
diatric intensive care, oncology, pulmonary medicine, metabolism and genetics, palliative and end-of-life care, and pathology) as well as an expert panel of nonmedical parent fac-
tulty members (parents of living and deceased children who serve
on a hospital advisory board). Recommendations from both pan-
els regarding the wording of and criteria for the classes of new
information were incorporated into the final scheme used in
this study (Table 2).

Table 1. Definitions of Criteria for Classes of Unexpected Finding or Clarification

<table>
<thead>
<tr>
<th>Class</th>
<th>Description</th>
<th>Criteria</th>
<th>Example*</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No unexpected finding or clarification</td>
<td>No unexpected finding or clarification</td>
<td>X</td>
</tr>
<tr>
<td>1</td>
<td>Major unexpected finding or clarification</td>
<td>Major findings include any principal underlying disease that contributed to the patient’s death that may or may not have been treated if known prior to the patient’s death (eg, malignant neoplasm that contributed to or caused the death, large pulmonary emboli, major infections)</td>
<td>X</td>
</tr>
<tr>
<td>2</td>
<td>Major unexpected finding or clarification not contributing to death</td>
<td>Major disease process that may have eventually required treatment or contributed to the patient’s death (eg, an undiagnosed malignant neoplasm, cirrhosis, or aneurysm that did not contribute to the patient’s death)</td>
<td>X</td>
</tr>
<tr>
<td>3</td>
<td>Minor unexpected finding or clarification</td>
<td>Secondary finding related to a principal underlying disease, therapeutic intervention, or diagnostic procedure (eg, hemorrhage, unsuspected metastases of a clinically known primary tumor)</td>
<td>X</td>
</tr>
<tr>
<td>4</td>
<td>Other minor unexpected finding or clarification</td>
<td>Other minor unexpected finding or clarification that might have eventually required treatment (eg, cholelithiasis, diverticulosis)</td>
<td>X</td>
</tr>
</tbody>
</table>

*Example A: A neonate with a suspected genetic metabolic syndrome, hypoxic-ischemic encephalopathy, renal failure, persistent hypertension, and mild lactic acidosis dies of cardiopulmonary arrest. On autopsy, he is found to have a mitochondrial disorder, renal tubular dysgenesis, acute bronchopneumonia, and a calcified pulmonary artery thromboembolus. He is also found to have cholestasis. Example B: An adolescent girl with cystic fibrosis in acute and chronic respiratory failure dies of pneumonia and candidiasis of the lung. On autopsy, she is found to have widespread pulmonary changes related to her cystic fibrosis as well as an acute bronchopneumonia. Example C: A neonate with irreversible pulmonary hypertension and respiratory failure dies. The clinicians have expressed concerns that the etiology is alveolar capillary dyslasia, a pulmonary disorder with questionable autosomal recessive inheritance. On autopsy, the neonate has severe pulmonary hypertensive changes with no indications of alveolar capillary dyslasia. He also has hepatomegaly with hepatocellular collapse.
hospital record (including attending physician admission, progress, and discharge notes; clinical assessments documented by allied medical staff; study results; and laboratory value reports) to create a premortem clinical summary for each case. Specifically, the following clinical data were collected for each decedent: (1) demographic information; (2) discussion of autopsy with guardian(s) documented in the patient record; (3) intensive care unit status during the final admission; (4) clinical cause(s) of death as recorded in the patient record, listed from a distal underlying cause of death to a proximal immediate cause of death; and (5) additional clinical diagnoses unrelated to the cause of death. Simultaneously and independently, a pathologist (L.M.E.) reviewed each final autopsy report to create a postmortem pathological summary for each case. Specifically, the following pathological data were collected for each decedent: (1) the extent of the autopsy (full and unrestricted; partial and restricted; or limited “metabolic autopsy” consisting only of biopsy samples collected immediately following death); (2) pathological cause(s) of death as recorded in the final autopsy report, listed from a distal underlying cause of death to a proximal immediate cause of death; and (3) additional pathological diagnoses unrelated to the cause of death. During the collection of information for the summaries, to assess independence, the clinician did not access the autopsy report data and the pathologist did not access clinical data in the hospital record. All data were recorded into a secure Microsoft (Redmond, Washington) Access database.

CLASSIFICATION OF CASES

On completing data collection, 3 reviewers (L.M.E., C.F., and J.A.F.) independently compared the recorded clinical and pathological causes of death, as well as any additional diagnoses unrelated to the cause of death, for each case. All premortem and postmortem discrepancies were classified according to the traditionally reported criteria (Table 1). For each case, the 3 raters also scored any additional information provided by the autopsy report using the family-centered new-information criteria (Table 2). In instances where raters’ results regarding added value differed (56 of the 100 cases), the classifications were settled by group discussion and unanimous consensus (L.M.E., C.F., and J.A.F.) in order to most closely replicate what occurs in the actual clinical setting. Of these 56 discordant cases, 38 of the final added-value scores were reduced to the most conservative score for that case. An expert physician trained in metabolism and genetics (J.G.) also assisted in determining the genetic implications of clinical and pathological findings.

DATA ANALYSIS

Statistical analyses were performed using Stata 9.2 software (StataCorp, College Station, Texas). Data were verified for accuracy before performing the analysis. Results were calculated using simple counts, percentages, and proportions. Exact confidence intervals were generated using the binomial distribution.

RESULTS

Of the 100 autopsy cases (Table 3), decedents had a median age of 0.4 year (range, 0–24 years) and 56% were male. The most frequent underlying causes of death were cardiovascular (22%) or genetic/congenital (19%) in nature. Seventy-nine percent of all decedents spent time in the intensive care unit during their terminal admission and the discussion of autopsy was documented on the medical record in 80% of the deaths. Most autopsies were
full and unrestricted (69%), as opposed to partial autopsies (26%), immediate postmortem biopsy samples only (2%), or unspecified (3%).

When we examined the 100 autopsy cases using the traditional criteria (Table 1), we found that major unexpected findings related to death occurred in 28% of the autopsies; minor unexpected findings or clarifications of major findings related to death were present in 48% of the autopsies (Figure 1).

When we examined the same 100 autopsy cases using our novel criteria (Table 2), we found new information that had the potential to offer families further explanations regarding the causes for their children’s deaths (53%); inform future reproductive choices of either the parents (20%; 95% CI, 3-56) or siblings (20%; 95% CI, 3-56); or affect the future health care provided to siblings (10%; 95% CI, 0-45). In comparison, autopsies of children who died of malignancy—a disease category in which a more definitive diagnosis might be made clinically—yielded new information with the potential to offer families further explanations regarding the causes for their children’s deaths (40%; 95% CI, 12-74). Similarly, those disease categories that contained cases requiring surgical intervention (in particular, cardiac conditions) or difficult diagnoses (such as metabolic or congenital/genetic) had an increased potential to provide institutions with data regarding quality assurance and quality control.

**Table 3. Characteristics of Sample**

<table>
<thead>
<tr>
<th>Demographic</th>
<th>Sample Size (N=100)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at death</td>
<td></td>
</tr>
<tr>
<td>&lt;1 mo</td>
<td>34</td>
</tr>
<tr>
<td>1-12 mo</td>
<td>23</td>
</tr>
<tr>
<td>1-6 y</td>
<td>19</td>
</tr>
<tr>
<td>9-15 y</td>
<td>13</td>
</tr>
<tr>
<td>15-24 y</td>
<td>11</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>M</td>
<td>56</td>
</tr>
<tr>
<td>F</td>
<td>44</td>
</tr>
<tr>
<td>Underlying cause of death</td>
<td></td>
</tr>
<tr>
<td>Neuromuscular</td>
<td>11</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>22</td>
</tr>
<tr>
<td>Respiratory</td>
<td>11</td>
</tr>
<tr>
<td>Renal</td>
<td>0</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>9</td>
</tr>
<tr>
<td>Hematologic/Immunologic</td>
<td>8</td>
</tr>
<tr>
<td>Metabolic</td>
<td>10</td>
</tr>
<tr>
<td>Malignancy</td>
<td>10</td>
</tr>
<tr>
<td>Genetic/congenital</td>
<td>19</td>
</tr>
<tr>
<td>Length of stay, d</td>
<td></td>
</tr>
<tr>
<td>0-1</td>
<td>31</td>
</tr>
<tr>
<td>2-7</td>
<td>24</td>
</tr>
<tr>
<td>8-28</td>
<td>24</td>
</tr>
<tr>
<td>&gt;28</td>
<td>21</td>
</tr>
<tr>
<td>Intensive care unit admission</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>79</td>
</tr>
<tr>
<td>No</td>
<td>21</td>
</tr>
<tr>
<td>Discussion of autopsy</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>80</td>
</tr>
<tr>
<td>No</td>
<td>20</td>
</tr>
<tr>
<td>Extent of autopsy</td>
<td></td>
</tr>
<tr>
<td>Full and unrestricted</td>
<td>69</td>
</tr>
<tr>
<td>Partial and restricted</td>
<td>26</td>
</tr>
<tr>
<td>Immediate postmortem biopsy samples</td>
<td>2</td>
</tr>
<tr>
<td>Unspecified</td>
<td>3</td>
</tr>
</tbody>
</table>

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On histological or gross anatomical investigation for definitive diagnosis—yielded new information with the potential to offer families further explanations regarding the causes for their children’s deaths (50%; 95% confidence interval [CI], 19%-81%); inform future reproductive choices of either the parents (20%; 95% CI, 3-56) or siblings (20%; 95% CI, 3-56); or affect the future health care provided to siblings (10%; 95% CI, 0-45). In comparison, autopsies of children who died of malignancy—a disease category in which a more definitive diagnosis might be made clinically—yielded new information with the potential to offer families further explanations regarding the causes for their children’s deaths (40%; 95% CI, 12-74). Similarly, those disease categories that contained cases requiring surgical intervention (in particular, cardiac conditions) or difficult diagnoses (such as metabolic or congenital/genetic) had an increased potential to provide institutions with data regarding quality assurance and quality control.

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**Figure 1.** Percentage of the 100 autopsies yielding unexpected findings/clarifications. See Table 1 for complete definitions and examples of the classes of unexpected findings/clarifications.

**Figure 2.** Percentage of the 100 autopsies yielding various types of new information. See Table 2 for complete definitions and examples of the classes of new information.
In this study, nearly 30% of pediatric autopsies yielded a major unexpected finding related to the cause of death, while even more frequently other minor unexpected findings or clarifications of major findings related to the cause of death were noted. Using a novel family-centered new-information classification scheme, we found that new information provided by autopsy most commonly had the potential to offer the families of deceased children further explanation regarding their child’s death. A third of cases yielded information that could guide improvements in hospital processes of care. In 1 of every 10 or 20 cases, the new information had the potential to impact the health care–related decisions of parents or siblings or advance general knowledge, respectively. Furthermore, the nature of the underlying disease process that resulted in death influenced both the type and probability of new information found at autopsy.

When considering the proportions of autopsies yielding new information reported in our study, 4 major limitations should be kept in mind. First, although we conducted a comprehensive medical record review for each case (including evaluation of the attending physician admission, progress, and discharge notes; clinical assessments documented by allied medical staff; study results; laboratory value reports; and the final autopsy report), the medical records used to compare premortem and postmortem findings may not completely capture the premortem and postmortem assessments of the involved clinicians and pathologists. Our estimates, however, of the percentage of autopsies with premortem and postmortem discrepancies match the figures reported by others, suggesting that our review of the clinical and pathological medical records captured information in a manner consistent with previous similar studies.

Second, the conduct of this study required the investigative team to make many subjective judgments, which could have biased the processes of data collection and data scoring. The classification of what constitutes an unexpected finding or clarification is a subjective determination that may differ among clinicians and pathologists. Similarly, what constitutes valuable new information is also a subjective determination that may differ among parents, clinicians, and pathologists. To safeguard against bias, we took several steps. Regarding data collection, we sought to minimize the risk of ascertainment bias by having the clinician and the pathologist operate independently: during the collection of information, the clinician who generated the clinical summary did not access autopsy report data and the pathologist who generated the autopsy summary did not access clinical data in the hospital record. Regarding scoring, we had explicitly defined the criteria used in this study to evaluate autop-

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Figure 3. Percentage of autopsies yielding various types of new information varies across causes of death. See Table 2 for complete definitions and examples of the classes of new information. A, Cardiovascular. B, Metabolic. C, Malignancy. D, Congenital.
sies, reducing the subjective component of both the traditional and the new-information classification schemes. Finally, using a group discussion format, we readily settled all discrepancies between raters by unanimous consensus; in the majority of these discrepancies, the most skeptical rater’s score for that case was assigned as the final score, decreasing the likelihood of scoring an autopsy finding as new information. Whether these steps were sufficient to nullify undue bias remains to be assessed, most likely by a litmus test of whether a different group of clinicians and pathologists would reach similar conclusions about a different set of autopsy cases.

Third, this study was performed at a major tertiary care academic children’s hospital. The population of children dying at this hospital, with severe and often complex underlying disease processes, is unlikely to be representative of the population of children who die at hospitals generally. Additionally, other local factors (such as institutional differences in the proportion of decedents who undergo autopsy, the likelihood that decedents with certain underlying conditions do or do not undergo autopsy, or the medical expertise of both the treating clinician and the examining pathologist) potentially affect the premortem and postmortem findings in a manner that limits our ability to generalize our findings to other institutions. Similarly, differences occurring over time (such as temporal trends in disease patterns or the development of new diagnostic modalities) may influence the proportion of autopsies that yield new information. To grapple with these limitations, each hospital could evaluate its own autopsy program using the family-centered new-information criteria and thereby enable physicians to use institution-specific data when counseling parents while also allowing for interinstitutional comparison of autopsy programs.

Finally, we report the findings from 100 autopsies, limiting the accuracy and precision of our reported percentages compared with what a larger sample of autopsies would have yielded. The overall sample size of 100 cases in particular limits the subanalyses stratified on the basis of the underlying cause of death, since each stratum had only a small number of autopsy cases. Nevertheless, despite limited statistical power, the major patterns identified when comparing the disease subcategories—such as the observation that autopsies performed on children with underlying metabolic and genetic disorders yielded different patterns of new information than autopsies performed on children with malignancy—are suggestive and warrant further scrutiny. We suggest that future evaluations of autopsy programs should use an ongoing review process of all autopsies to maximize sample size so that findings across all cases and within subgroups are as accurate and precise as possible.

These limitations notwithstanding, to our knowledge, this study is the first of its kind to provide a set of family-centered criteria that can be used to evaluate autopsy programs in terms that are relevant to the parents of dying children. By shifting the paradigm of autopsy program evaluation from using institution-centered criteria to using family-centered criteria, institutions will empower both clinicians and the parents of dying children to make better-informed decisions regarding autopsy. With institution-specific data in hand, clinicians will likely feel more confident when counseling the parents and families of dying children regarding autopsy. Specifically, we recommend expressing the expected utility of autopsy not as a proportion or percentage (which are rather abstract concepts) but instead as a “natural frequency” of the number of autopsies needed to yield the type of new information. This can be illustrated using the data we report, where 1 of every 2 pediatric autopsies performed had the potential to offer parents further explanation regarding their child’s death and 1 of every 10 pediatric autopsies performed had the potential to impact parents’ future reproductive choices. Additionally, discussion of the pros and cons of autopsy using specific, explicit, and understandable terms may reduce or eliminate the common misconceptions surrounding the practice of autopsy.

Institutions may also benefit from using family-centered autopsy evaluation programs. Using both the traditional and the new-information criteria, the constant review of autopsy cases can be performed efficiently by the clinician and pathologist at the time of autopsy; formalizing this process may also enhance the dialogue between clinicians and pathologists, potentially accelerating improvements in quality of care and increasing the communication of autopsy results to the parents of deceased children. In the coming decade, decision making about autopsy is likely to be influenced by technical advances in both premortem and postmortem diagnostic procedures and the allure of a noninvasive autopsy. The metabolic autopsy, which involves the biopsy collection of tissue within an hour of death for additional diagnostic metabolic or genetic testing, has been shown to successfully identify an undiagnosed metabolic disease in 18% of cases, and in our case series, this procedure demonstrated at least 1 metabolic disorder (Table 1 and Table 2). The metabolic autopsy, though, not only requires the hospital to have the staff and equipment to conduct such an autopsy but also must be performed immediately after death, which may interfere with parental grieving. Thus, although offering potentially revelatory diagnostic information in cases of suspected metabolic causes of death, the metabolic autopsy has its own set of risks and benefits that parents and clinicians must consider. Similarly, as new and less invasive diagnostic modalities become available and reliable (such as biobanking premortem or postmortem tissue or blood samples for future diagnostic testing as new tests become available or performing so-called virtual autopsies involving advanced postmortem radiographic or magnetic resonance imaging studies), the discussion between a decedent’s family and the clinician regarding each modality’s risks and benefits will need to adapt accordingly. Even with less invasive means to collect premortem and postmortem data, however, our family-centered criteria can still be used to evaluate new diagnostic modalities in terms that are relevant to the families of dying children.

Ultimately—and rightly—the authority to make the decision of whether to pursue pediatric autopsies resides with the parents. If hospitals were to conduct evaluations of their autopsy programs using family-centered criteria, we believe that parents could better partner with clinicians to identify the types of new information that might be important to them and then use the reported data to exam-
ine the likelihood that autopsy would yield the desired new information given their child’s particular condition.

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Author Contributions: Dr Feudtner, the principal investigator, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Feinstein, Ernst, and Feudtner. Acquisition of data: Feinstein and Ernst. Analysis and interpretation of data: Feinstein, Ernst, Ganesh, and Feudtner. Drafting of the manuscript: Feinstein. Critical revision of the manuscript for important intellectual content: Feinstein, Ernst, Ganesh, and Feudtner. Statistical analysis: Feinstein and Feudtner. Obtained funding: Feudtner. Administrative, technical, and material support: Feudtner. Study supervision: Ernst and Feudtner.

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REFERENCES