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PAPER

PATHOLOGY AND BIOLOGY

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Natural, Unexpected Deaths: Reliability of a Presumptive Diagnosis*

ABSTRACT: We retrospectively analyzed 100 deaths because of suspicions and concerns expressed by the family. We compared the preautopsy cause of death, as determined by a thorough review of the clinical data and circumstances, to the autopsy-derived cause of death. In the majority (91/100), the preautopsy and postautopsy proximate causes of death were in agreement. In 9%, the autopsy provided information that resulted in a proximate cause of death different than anticipated. In four instances, the manner of death also was incorrect and was determined to be an accident rather than the originally presumed natural. No homicide or suicide would have been misclassified. In another nine instances, where the premortem and postmortem proximate causes of death were in agreement, the autopsy provided a specific mechanism of death. With a quality initial medicolegal death investigation, a subset of sudden deaths in adults may be reliably certified without an autopsy.

KEYWORDS: forensic sciences, forensic pathology, autopsy, discrepancy, death certificate

Despite technological advances in medical practice in recent decades, the autopsy, in combination with a competent investigation of the medical history and circumstances of the death, is still considered the gold standard for determining the cause and manner of death. In the United States, however, the majority of decedents do not undergo autopsy (1). The rates of autopsies performed in hospitals have dropped to alarmingly low levels over the past 40 years (1–4). Most would agree that with the current state of hospital and forensic pathology facilities and staffing in addition to religious and cultural objections to autopsy, a majority national autopsy rate in the United States is unlikely. Therefore, one must accept that the majority of deaths are certified without an autopsy, and, therefore, misdiagnoses are inevitable.

The goal of physicians is to minimize these misdiagnoses by using their knowledge and experience to select which decedents should have an autopsy and which can be certified without an autopsy. Because of the mission of the medical examiner/coroner (ME/C), their focus also is to ensure that the *manner* of death is correct (i.e., a homicide is not certified as a natural death). This concern may subordinate the investigation of natural deaths to unnatural deaths (homicide, suicide, and accident). Most would rather hazard misdiagnosing a death because of bicuspid aortic stenosis as atherosclerotic cardiovascular disease than to miss a homicide by not performing an autopsy. The manner of death not only has ramifications for the criminal justice system but also for the next of kin with regard to civil matters such as life insurance and pension benefits.

Many clinicians, who issue a large percentage of these death certificates, do not fully understand what constitutes a medicolegal reportable death or a competent death certificate, leading to inaccurate death certificates (5–12). A recent study of deaths certified at an academic medical center found that 34% of the certificates had no proximate cause or the wrong cause or manner of death (6). These errors were not based on findings from an autopsy (none of these decedents had an autopsy) but rather they were found by an independent chart review (6). Even if the information is available to allow a competent determination of the cause of death to be made without an autopsy, it still may be incomplete or incorrect. Common errors include listing the mechanism or immediate cause of death without the underlying (proximate) cause and the failure to recognize a delayed death due to injury.

ME/C offices commonly receive inquiries from family members of a decedent about a death in which the initial review did not appear to warrant an autopsy. Offices around the country handle these inquiries differently. In New York City, if a family member inquires about an autopsy because of a suspicion or concern about the unexpectedness of a death, an autopsy by the Office of Chief Medical Examiner (OCME) may be justified. In fact, the majority of these inquiries involve fatalities that would have undergone autopsy even without the suspicions expressed by the family. A small percent of these fatalities, however, have an initial history and circumstances that would not have necessitated an autopsy if there had not been the later expressed suspicion. We reviewed 100 such fatalities in which an autopsy was performed subsequently. The goal of this study was to determine how accurate death certification based upon the history and circumstances is when compared with the cause of death disclosed by the autopsy in these select instances.

Materials and Methods

The New York City Office of Chief Medical Examiner (NYC OCME) investigates all unexpected, violent, and suspicious deaths in New York City. The NYC OCME employs 33 medical examiners distributed at five facilities (one in each of the five boroughs of New York City). The main administrative offices and toxicology,

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forensic biology (DNA), and histology laboratories are located in the Manhattan facilities. Reported deaths are initially investigated by an OCME medicolegal investigator (MLI). The majority of these investigators are physician assistants. The remaining are physicians. They determine whether a death is a medical examiner case (i.e., brought into the office for further evaluation) or if it may be released to the funeral home with certification by the primary care physician. If the death occurs outside of a hospital, the MLI visits the scene and examines the body. The MLI creates a report describing the medical history and circumstances. The medical examiner then reviews these reports as well as scene photographs, hospital reports, and/or police reports, in order to determine if an autopsy is necessary.

From August 2006 to February 2008, there were 2272 deaths certified by the Bronx office of the NYC OCME of which 1733 underwent autopsy (76%). The certified deaths included: 1170 naturals; 107 therapeutic complications; 589 accidents; 240 homicides; 106 suicides; and 60 undetermined manners. Of these deaths, those in which the family specifically inquired about an autopsy were prospectively tracked. The telephone notice of death and initial MLI's report were examined for each of these decedents. The goal was to obtain an autopsied cohort of 100 sudden, apparent natural, out-of-hospital deaths in which the medical examiner may not have performed an autopsy but for the suspicions raised later by the family. Based upon the initial investigative reports, a preautopsy cause and manner of death were determined for this study. These were compared with the cause and manner of death determined by the autopsy. In none of these 100 deaths was there a known history of recent trauma, substance or alcohol abuse, psychiatric illness (depression), and recent surgery or hospitalization.

We reviewed the initial investigative reports of 346 family inquiries in order to obtain the cohort of 100 deaths. Based upon the review of the history and circumstances, 246 of these 346 deaths typically would have undergone autopsy examination or were pronounced dead more than 1 h after arrival at the emergency department. Deaths that usually would have undergone autopsy included any history of recent trauma, substance or alcohol abuse, psychiatric illness (depression), or recent surgery or hospitalization. Typically, the presence of any of these findings would have resulted in an autopsy.

The proximate (underlying) cause of death is the etiologically specific, underlying medical condition or injury that initiates the lethal sequence of events (13). A competent cause of death statement requires the proximate (underlying) cause (14). The proximate cause is defined as that which in a natural and continuous sequence, unbroken by any efficient intervening cause, produces the fatality and without which the end result would not have occurred. The cause of death also may include an immediate cause and mechanism of death; however, only the proximate cause of death is required to be listed on the death certificate. Immediate causes of death are complications and sequelae of the underlying cause interposed between the proximate cause and the fatal result (e.g., bronchopneumonia, pulmonary embolism). Mechanisms of death are etiologically nonspecific physiologic chains of events that connect the cause of death to the moment of death (e.g., exsanguination, congestive heart failure, arrhythmia). Immediate causes and mechanisms may not stand alone on a death certificate; they require an underlying (proximate) cause of death (14).

The manner of death is determined from the cause and circumstances of death. The manners of death listed on the New York City Certificate of Death include: natural, accident, therapeutic complication, suicide, homicide, and undetermined. A preponderance of medical evidence (probability) is the degree of certainty required by vital statistics bureaus for opinions expressed on death certificates (13), but our standard for the certification of homicide or suicide is certainly beyond a reasonable doubt.

Contributing conditions are additional disorders listed on the death certificate as contributory to death but unrelated to the underlying cause of death. Typically, contributory conditions are listed in *part 2* of the death certificate; they should not be woven into the primary cause of death statement along with the proximate cause (14).

An autopsy at the NYC OCME consists of an external examination followed by an internal examination of the head, neck, and thoracic, abdominal, and pelvic cavities as well as toxicologic analysis. Radiographs, histologic examinations, microbiology cultures, and formal neuropathologic examinations (on the formalin-fixed brain by a neuropathologist) are performed at the discretion of the prosector.

Arteriosclerotic cardiovascular disease (ASCVD) includes ischemic cardiovascular disease caused by atherosclerosis and small vessel disease (hypertensive cardiovascular disease [HCVD]). Hypertensive and atherosclerotic cardiovascular disease commonly occur in the same patient. Individuals also may die from pure HCVD with normal coronary arteries or from coronary artery atherosclerosis with no evidence of hypertensive disease. Distinguishing between these two types of heart disease may have important clinical implications. For the purpose of this study, however, disagreements between these two diagnoses in the preautopsy and postautopsy certifications were not considered as differences. For example, if the preautopsy diagnosis was ASCVD and the autopsy diagnosis was HCVD, this was not considered a difference.

Results

Between August 2006 and February 2008, *c.* 20% of all autopsies performed in the Bronx office of the NYC OCME had a family inquiry about the death (346/1733). Most of these (71%, 246/346) had an autopsy performed due to the decedent's medical history and/or circumstances surrounding the death. Only 5.7% of autopsies (100/1733) were performed due to the concerns and suspicions raised by the decedent's family.

The causes and manners of death for the preautopsy and postautopsy certifications are in Table 1. Of these 100 autopsies, the preautopsy proximate cause of death was correct in 91% (91) of the fatalities. In 9% (9/100), the autopsy revealed a different cause of death than the one predicted. The manner of death was correct in 96% (96) instances. Of the incorrect manners of death, all four were accidents due to acute intoxications. No suicide or homicide would have been misdiagnosed. The circumstances and final certifications of the incorrect preautopsy death certifications are in Table 2.

The age ranged from 26 to 93 years (mean = 63 years) and the racial/ethnic breakdown included 49 Black, 39 Hispanic, 11 White,

TABLE 1—*Proximate causes of death before and after the autopsy.*

Proximate Cause of Death	Preautopsy	Postautopsy
Arteriosclerotic cardiovascular disease	31	14
Arteriosclerotic and hypertensive cardiovascular disease	29	36
Hypertensive cardiovascular disease	27	27
Bronchial asthma	7	7
Diabetes mellitus	1	2
Metastatic malignancy	4	7
Acute intoxication	0	4
Ruptured cerebral artery aneurysm	0	1
Postpartum cardiomyopathy	1	1
Bronchial asthma/emphysema and hypertensive cardiovascular disease	0	1
Total	100	100

TABLE 2—*Nine deaths in which the preautopsy certification differed from the autopsy-based certification*.*

	History	Preautopsy Proximate Cause	Postautopsy Proximate Cause
1	57-year-old man with a history of hypertension and diabetes mellitus who was found unresponsive by his daughter. He was last seen alive the night before without complaints. There was no history of drug or alcohol abuse. His medications included furosemide, lisinopril, insulin, and metoprolol.	Hypertensive cardiovascular disease	Acute cocaine intoxication
2	57-year-old woman with a history of hypertension, coronary artery disease (status-post coronary by-pass surgery, remote), congestive heart failure, and pulmonary emphysema/asthma. She had been discharged 6 weeks earlier following treatment of a bronchopneumonia due to her worsening chronic obstructive pulmonary disease. On the morning of her death, she did not appear well to her daughter who later found her dead in bed when she returned home.	Pulmonary emphysema/Asthma	Bronchopneumonia complicating metastatic laryngeal squamous cell carcinoma
3	55-year-old man with a history of insulin-dependent diabetes. According to his nephew, he complained of feeling weak and went into the bathroom were he was later found unresponsive. He was pronounced at the scene. There was no history of alcohol or drug abuse.	Arteriosclerotic cardiovascular disease	Acute cocaine intoxication
4	52-year-old man with a history of insulin-dependent diabetes mellitus and a ''cardiac condition'' was found dead in bed. A few days earlier he had complained of not feeling well and saw his primary care physician who prescribed an antihypertensive medication.	Hypertensive cardiovascular disease	Diabetic ketoacidosis
5	62-year-old woman with a history of arthritis was found dead in bed by her son who lived with her. She had complained of shortness of breath and vomiting the day before her death. Following the toxicology analysis, the husband stated that 2 days prior to her death she had been started on a fentanyl patch (75 μg/h) by her physician. During those next 2 days she had complained of somnolence and shortness of breath.	Arteriosclerotic cardiovascular disease	Acute fentanyl intoxication
6	49-year-old woman with a history of hypertensive cardiovascular disease with congestive heart failure, insulin-dependent diabetes, asthma, obesity, and arthritis (for which she uses a wheelchair) died at home. She had been admitted and released from the hospital over 1 week prior to death. Her discharge diagnosis was congestive heart failure that had responded to diuretics. Her medications included: diovan and lasix. Her primary care physician was willing to certify the death.	Hypertensive cardiovascular disease	Acute cocaine intoxication
7	61-year-old woman with a history of hypertensive cardiovascular disease, diabetes, and asthma was recently treated for a urinary tract infection. The decedent was last seen by her husband in the morning after breakfast. He found her dead in bed later in the day.	Hypertensive cardiovascular disease	Ovarian carcinoma
8	55-year-old man with no recent medical problems was last seen by his son in the morning. He was in his usual state of good health. He was found later that day dead on the apartment floor. He took low-dose aspirin. There was no history of alcohol or drug abuse and no evidence of injury or foul play.	Arteriosclerotic cardiovascular disease	Ruptured cerebral artery aneurysm
9	71-year-old man with a history of hypertension and noninsulin-dependent diabetes was found dead at home. Medications included metformin and lisinopril.	Hypertensive cardiovascular disease	Pulmonary embolism due to metastatic colon carcinoma

*Part 2, contributing conditions, not included.

and one Asian. There were 54 men and 46 women. The location where the decedent was pronounced dead was: 72 residence, 19 emergency department (all within 1 h of arrival), and 10 nursing home. Eleven of the decedents were nursing home/long-term care facility residents. The family members who made the inquiry included: 26 daughters, 20 sons, 15 siblings, 14 wives, six husbands, eight uncles/nieces/nephews, five mothers, four grandchildren, and two multiple relatives.

In an additional nine instances, where the proximate cause of death and manner of death were correctly predicted, the autopsy was able to provide further information about the mechanism or immediate cause of death. These included myocardial infarcts (3), intracerebral hemorrhage (3), pulmonary embolism (1), bronchopneumonia (1), and aortic dissection (1).

Discussion

Neither forensic pathologists nor clinical physicians are held to the standard of being correct 100% of the time with their diagnoses and death certifications (15). Even in a homicide trial, in which the accused may be eligible for the death penalty, forensic pathologists are not required to be certain of their findings beyond a possible doubt. For natural deaths, the standard is probability (i.e., more likely than not). Numerous quality assurance studies have examined discrepancies between the autopsy and the clinical diagnoses (1,5,16–24). Most of these studies involve hospitalized patients. The addition of ''hospitalization'' to the equation may improve the accuracy due to diagnostic testing but it also may complicate the diagnoses in others due to potential therapeutic complications (25). Therefore, we selected 100 instances in which persons were pronounced dead at home, in a nursing home, or within 1 h of arrival at the emergency department. Our study revealed that in nine of those 100 fatalities, the cause of death without an autopsy would have been incorrect. In addition, in nine more instances, where the proximate cause of death was correctly predicted, the autopsy further elucidated the immediate cause and mechanism of death.

A similar study was performed by Lundberg and Voigt on 100 sudden unexpected adult deaths in Sweden where the autopsy rate exceeds 90% in some regions (17). They theorized that if one had diagnosed the cause of death as ischemic/coronary artery disease,

it would have been correct in only 49% of the deaths. Their study had two problems. The first involved the broad selection criteria. They did not provide the age range of the decedents, except to state that for inclusion they needed to be over 18 years of age (there are few physicians who would certify the sudden death of a 23-year-old man with no known medical history as ischemic heart disease without an autopsy). Their criteria also excluded deaths with: suspicion of an unnatural manner after "careful police investigation," hospitalization immediately before death, and any evidence of trauma "by external exam."

The second problem with their study was their list of autopsy-determined causes of death. They did not include a proximate cause in 36 deaths (just the mechanism or immediate cause). This is a common mistake, particularly among clinicians who tend to focus on immediate causes and mechanisms of death as opposed to the underlying (proximate) cause. For the cause of death, their list included: pulmonary embolism, hepatitis with massive necrosis, bronchopneumonia, and subarachnoid hemorrhage. None of these is an etiologically specific disease and is not an acceptable, competent cause of death. Among these 36 deaths, there are 20 in which the mechanisms or immediate causes may be because of atherosclerotic/hypertensive cardiovascular disease (e.g., aortic dissection, intracerebral hemorrhage, and cardiac hypertrophy). If these findings were properly classified by proximate cause of death, their number of missed certifications would have decreased.

Three other studies also have examined the accuracy of the determination of the cause of death without autopsy examination (20,26,27). An Australian study retrospectively examined 261 deaths that had undergone autopsy (26). They assigned a natural cause of death based upon the preautopsy investigation and compared those determinations with the actual autopsy findings. The cause of death was incorrect in 28% of deaths and 3% had an unnatural manner. This study did not provide a proximate cause in 41 (16%) deaths which included: acute intracerebral hemorrhage, aortic dissection/aneurysm, acute pancreatitis, and pulmonary thromboembolism. Among the 74 causes that were misdiagnosed, they did not include a proximate cause in at least 35 deaths including 13 acute intracerebral hemorrhages, 11 pulmonary thromboemboli, five bronchopneumonia, and three acute pancreatitis. Chronic alcoholics also were included in this study, one of whom died of blunt head injury discerned at autopsy. Among the misdiagnosed unnatural deaths (3%), there were four drug intoxications, one blunt trauma, and one choking. Six malignancies and two diabetics initially were not diagnosed.

In current use, ASCVD has become the default cause of death for sudden, apparent cardiac deaths in the middle-aged and elderly populations in which an autopsy is not performed. In its broadest sense, it includes ischemic cardiovascular disease caused by atherosclerosis and HCVD with small vessel disease. In fact, arteriosclerosis is strictly defined as thickened, hardened vessels, and three patterns are recognized: atherosclerosis, arteriolosclerosis (associated with hypertension), and Mönckeberg medial calcific sclerosis (28). Sequelae of these proximate causes include cerebral infarcts/hemorrhages, aortic dissections, congestive heart failure, myocardial infarcts, and end-stage kidney disease. The use of ASCVD is sufficient to include these numerous immediate causes and mechanisms. One hazard of this term, however, is that physicians may sacrifice a thoughtful and careful death investigation and indiscriminately use ASCVD as a catch-all diagnosis for any sudden death.

We demonstrate that with a competent medicolegal investigation (not just relying on "careful police investigation"), in combination with sound clinical judgment, forensic pathologists would have the correct proximate cause of death over 90% of the time in our cohort. With routine toxicologic analysis including vitreous electrolyte testing on external examinations, this percent would be even higher. If this testing had been peformed in this cohort, an additional five of the nine missed diagnoses (four intoxications and one diabetic ketoacidosis) would have been detected.

A selection bias may be involved with these autopsies. For example, a family may be concerned about a possible drug intoxication but are unwilling to share this information with the MLI. Instead, they express a suspicion about the death in order to stimulate further investigation. This scenario would increase the likelihood that the subsequent autopsy would detect an unexpected cause of death (such as a drug intoxication).

With regard to an age bias, our study was not limited to the elderly who have a high incidence of ASVCD (29). The average age was 63 years and the youngest was a 26-year-old man who died at home from metastatic osteosarcoma. There also was a 35-year-old decedent with a well-established history of asthma (which had required previous hospitalizations) who had a witnessed asthma exacerbation at home and died en route to the hospital. In both instances, the toxicology was noncontributory.

Although the autopsy did not change the cause (or manner) of death in 91% of these deaths, in some instances it helped further elucidate the immediate cause or mechanism of death. Determination of the mechanism of death may have importance to other parties beyond the determination of the proximate cause. For example, a patient is diagnosed with a small abdominal aortic aneurysm and surgery is deferred. Several weeks or months later the patient is found dead at home. Did this patient die of a ruptured aneurysm or from cardiac disease? Although the proximate cause of death may not change, the mechanism and immediate cause of death would.

Eleven of the decedents had been residents of nursing homes/long-term care facilities when they died. People in long-term care facilities usually have a well-established medical history and access to medical care. If they die in the nursing home, there usually is a primary care physician available to certify the death without involvement of the ME/C. Therefore, if such a death is reported to the ME/C, it commonly indicates that something suspicious or unusual has happened. Nursing home residents with poor health and functional impairments are at increased risk for neglect and abuse (30). The ME/C would be wise to investigate these deaths. Concerns of abuse and neglect may arise much later when the body has already been interred or cremated and it is too late to perform an autopsy. Ignoring suspicions in these instances puts the ME/C in a difficult position when these allegations surface.

Some pathologists may refuse to perform an autopsy because of professional reasons. Sound medical practice involves determining what tests are necessary and how they may change medical decision making. Just as clinical physicians should not order tests that do not affect treatment or diagnosis, some believe that autopsies should not be peformed unless absolutely necessary. If a pathologist can determine the cause of death without an autopsy, should one be done? The value of the autopsy is not only to determine the cause of death. For example, a homicidal gunshot wound of the head usually does not require an autopsy to determine the cause of death but an autopsy is required for other medicolegal reasons (e.g., recovery of ballistic evidence, determination of the mechanism of death, reconstruction of the fatal episode, etc.).

There are numerous other valid reasons why some families are in favor of autopsies. The family's questions and concerns should not be ignored. Families have varying reactions to the death of a loved one: grief, anger, confusion, fear, and guilt are some. Their request for an autopsy can be extremely difficult for some people,

and, therefore, a family's suspicions should not be taken lightly. It is not rare for forensic pathologists to be contacted by a family inquiring about the death of a loved one that happened years earlier and in which an autopsy was never performed. As time passes, those suspicions persist, and time after time it confirms that the best opportunity to attempt to address those suspicions would have been shortly after death by the performance of an autopsy.

The ethics of this decision for the pathologists are further complicated if they are remunerated on a "per case" basis. That is, they receive a fee per autopsy. In these situations, if the pathologist is responsible for deciding whether an autopsy will or will not be carried out, there is a conflict of interest. A conflict of interest exists even if no unethical or improper act results from it. A conflict of interest can create an appearance of impropriety that can undermine confidence in the system. Should the ME/C who makes the autopsy determination have a personal monetary stake in the outcome of the decision? Autopsies generally require much more work and time than it takes to certify a death without an autopsy. Therefore, salaried pathologists with no financial stake in the procedure, clearly do not perform autopsies for monetary or trivial reasons but because in their judgment an autopsy is required to satisfy their public duty and professional obligations.

To summarize, with a quality initial medicolegal death investigation, a subset of sudden deaths in adults may be reliably certified without an autopsy. Excluded from this cohort are any decedents with recent trauma, substance or alcohol abuse, psychiatric illness (depression), and recent surgery or hospitalization. The use of toxicology testing in combination with a competent external examination would further improve death certification accuracy. Although these deaths may be reliably certified with an autopsy, performance of an occasional autopsy on this subset of deaths because of suspicions raised by the next of kin should be considered. These instances add a small percent of additional autopsies and the benefit to the family is immeasurable.

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