Virtual Autopsy With Multiphase Postmortem Computed Tomographic Angiography Versus Traditional Medical Autopsy to Investigate Unexpected Deaths of Hospitalized Patients

A Cohort Study

Dominic Wichmann, MD, DTM*; Axel Heinemann, MD*; Clemens Weinberg, MSc; Hermann Vogel, MD, PhD; Wilhelm Wolfgang Hoepker, MD, PhD; Silke Grabherr, MD, PhD; Klaus Pueschel, MD, PhD; and Stefan Kluge, MD

Background: “Virtual” autopsy by postmortem computed tomography (PMCT) can replace medical autopsy to a certain extent but has limitations for cardiovascular diseases. These limitations might be overcome by adding multiphase PMCT angiography.

Objective: To compare virtual autopsy by multiphase PMCT angiography with medical autopsy.

Design: Prospective cohort study. (ClinicalTrials.gov: NCT01541995)

Setting: Single-center study at the University Medical Center Hamburg–Eppendorf, Hamburg, Germany, between 1 April 2012 and 31 March 2013.

Patients: Hospitalized patients who died unexpectedly or within 48 hours of an event necessitating cardiopulmonary resuscitation.

Measurements: Diagnoses from clinical records were compared with findings from both types of autopsy. New diagnoses identified by autopsy were classified as major or minor, depending on whether they would have altered clinical management.

Results: Of 143 eligible patients, 50 (35%) had virtual and medical autopsy. Virtual autopsy confirmed 93% of all 336 diagnoses identified from antemortem medical records, and medical autopsy confirmed 80%. In addition, virtual and medical autopsy identified 16 new major and 238 new minor diagnoses. Seventy-three of the virtual autopsy diagnoses, including 32 cases of coronary artery stenosis, were identified solely by multiphase PMCT angiography. Of the 114 clinical diagnoses classified as cardiovascular, 110 were confirmed by virtual autopsy and 107 by medical autopsy. In 11 cases, multiphase PMCT angiography showed “unspecific filling defects,” which were not reported by medical autopsy.

Limitation: These results come from a single center with concerted interest and expertise in postmortem imaging; further studies are thus needed for generalization.

Conclusion: In cases of unexpected death, the addition of multiphase PMCT angiography increases the value of virtual autopsy, making it a feasible alternative for quality control and identification of diagnoses traditionally made by medical autopsy.

Primary Funding Source: University Medical Center Hamburg–Eppendorf.


For author affiliations, see end of text.

*Drs. Wichmann and Heinemann contributed equally to this work.

Medical autopsy has been the gold standard for quality control in clinical medicine for more than a century (1), but clinicians miss approximately 15% of diagnoses despite advances in diagnostic techniques (2–7). Relatives who decline an autopsy request, reimbursement issues, changes in clinical workflows, faith in modern diagnostic techniques, and fear of litigation for missed diagnoses have contributed to the worldwide decline in autopsy rates over the past decades (8–11). Virtual autopsy by multiphase imaging using postmortem computed tomography (PMCT) in conjunction with software for 3-dimensional visualization is a recent innovation that may overcome such obstacles.

Initial studies have shown that PMCT is often an accurate imaging technique for providing a cause of death in patients who died in the intensive care unit or outside the hospital (4, 12). However, these studies have also identified a major restriction of PMCT. Because of the cessation of circulation, PMCT is of limited value for detecting pulmonary embolisms, which account for up to 15% of clinically missed diagnoses identified in routine autopsies (13), and cardiovascular events, which are the leading cause of death in industrialized countries (14, 15). Postmortem angiography in combination with CT is a recent innovation to overcome such obstacles.

Of several protocols described (16–19), multiphase PMCT angiography (20) is a highly standardized technique that has been shown to produce reliable results when compared with medical autopsy in the context of trauma patients in forensic medicine (21). However, experience in hospitalized patients is scarce. Therefore, the aim of our study was to compare multiphase PMCT angiography with medical autopsy in a setting of emergency and intensive care medicine in patients who died unexpectedly or within 48 hours of an event necessitating cardiopulmonary resuscitation (CPR).

Methods

Study Design

Between 1 April 2012 and 31 March 2013, we compared the findings of virtual autopsy, including multiphase
Virtual Autopsy

Virtual autopsy was done at the Department of Legal Medicine using a Philips MX8000 4-slice CT scanner and a Philips Brilliant 16-channel CT scanner (Philips Healthcare, Best, the Netherlands). It consisted of native PMCT without angiography, followed by multiphase PMCT angiography of the head, neck, chest, abdomen, and hip joints. For the multiphase PMCT angiography, the protocol from Grabherr and colleagues (20) was used with minor variations. After cannulation of the femoral vein and artery with a 3/8-inch cannula, paraffin oil containing 6% Angiofill (Fumedica, Muri, Switzerland) was injected by means of a modified heart–lung machine.

Perfusion was divided into 3 phases. In the first (arterial) phase, 1200 mL of contrast medium was injected at a rate of 800 mL/min via the femoral artery. Arterial CT of the head, thorax, and abdomen was done with a slice thickness of 1 mm and a pitch of 0.8 mm. To enhance the sensitivity for pathologic conditions of the coronary vessels, targeted scanning of the heart was done with a slice thickness of 0.8 mm and a pitch of 0.4 mm.

In the second (venous) phase, a retrograde injection of 1600 mL of contrast medium at a rate of 800 mL/min via the femoral vein was done, followed by CT of the venous system using the same variables as for the arterial scan. During the final (dynamic) phase, artificial circulation with 200 mL of contrast medium was generated at a rate of 500 mL/min by injection via the arterial cannula and application of a vacuum to the venous cannula. In contrast to the arterial and venous phases, scanning was done during the ongoing injection to mimic in vivo conditions.

As a variation from this standard protocol, we administered an extra 1000 mL of contrast medium in the venous and dynamic phases in patients with a body mass index greater than 30 kg/m². Angiographic examinations were done on a regular basis each Monday, Tuesday, and Friday, at the earliest convenience.

Classification of Radiologic Findings

A board-certified radiologist with considerable experience reading postmortem images reviewed the cases. The radiologist had access to all clinical records and the death certificates but was unaware of the findings of the medical autopsy (which was done afterward). A second expert in the field crosschecked all angiographic findings. Computed tomographic data were processed using OsiriX, version 5.6 (Pixmeo, Geneva, Switzerland). Animated videos (Supplements 1 to 3, available at www.annals.org) were processed with Final Cut Pro X, version 10.0.8 (Apple, Cupertino, California).

Medical Autopsy and Histologic Examination

Full medical autopsy with histologic examination according to the hospital’s institutional standards was done after virtual autopsy by residents from the Department of Legal Medicine and the Department of Pathology supervised by a board-certified senior pathologist. The pathologists had access to all clinical records and the death certificates but were unaware of findings from the virtual autopsy. Restricted autopsies focusing on the presumed organ system of interest are not routinely practiced in our institution and therefore were not done.

Classification of Autopsy Findings

Two board-certified internists reviewed the clinical records for clinical diagnoses made before deaths and compared these with the reports from the virtual and medical autopsies. If the reviewers’ assessments agreed, the review process was complete. All cases with discrepant findings were crosschecked. In cases of uncertainty or disagreement (3 cases), consensus was achieved through mediation by a pathologist and a specialist in the field of interest.

New diagnoses from virtual or medical autopsy were classified as major or minor on the basis of institutional standards (4), which had been adapted from the criteria of Goldman and associates (22) and Dimopoulos and coworkers (23). New major diagnoses were those that could have contributed substantially to the outcome or those for which detection before death would have resulted in a...
change of treatment and potential clinical benefit for the patient. New minor diagnoses were clinical conditions that might have been related to the final condition but did not contribute to death. The decision to classify a new diagnosis as major or minor depended on the individual clinical situation. For example, pneumothorax due to lung injury caused by traumatic rib fractures during CPR in a person with fulminant pulmonary thromboembolism would have been classified as minor, whereas pneumothorax resulting in cardiac arrest after an unsuccessful attempt to place a central venous line would have been classified as major.

Antemortem diagnoses that did not translate directly into radiologic or morphologic pathologic conditions (for example, electrolyte imbalances or cardiac arrhythmias) and diagnoses without clinical relevance (for example, benign renal cysts) were not included in the analysis. For angiographic findings (especially those involving the coronary arteries), major vessels and first-grade branches were included in the analysis.

Statistical Analysis
All data were analyzed with Statistica, version 6.0 (StatSoft, Tulsa, Oklahoma). Data that were normally distributed are presented as means (SDs), and data outside the normal distribution are presented as medians (ranges). Venn diagrams were constructed with eulerAPE, version 3.0.0 (University of Kent, Canterbury, United Kingdom) (24).

Role of the Funding Source
The study was funded chiefly by the University Medical Center Hamburg–Eppendorf. Funding was also provided by the Fondation Leenaards. Fumedica provided consumables for multiphase PMCT angiography to the Institute of Legal Medicine. The funding sources had no influence on the design, execution, or analysis of the study; on the preparation of the manuscript; or the decision to submit the manuscript for publication.

RESULTS
Study Group
Of 143 cases meeting the inclusion criteria, virtual and medical autopsy were done in 50 hospitalized patients (35%). Of the patients excluded from the study, relatives declined informed consent in 71 cases, 12 were excluded because of maintenance work on the CT scanner, and 10 were excluded because funerals were scheduled before an autopsy could be done (Appendix Figure 1, available at www.annals.org). The mean age of included patients was 70 years (SD, 12) (range, 27 to 84 years), and 76% were men. Thirty-one patients died within 48 hours after CPR, and 19 patients had an unexplained deterioration in clinical status rapidly resulting in death while in the intensive care unit. A medical or neurologic condition was the cause of hospitalization in 35 patients, and surgical procedures were the cause in the remaining 15. The median interval between death and the CT scan was 4 days (range, 1 to 6 days), and the interval between death and medical autopsy was 6 days (range, 2 to 9 days).

Diagnoses From Clinical Records, Virtual Autopsies, and Medical Autopsies
Clinical records showed that 336 diagnoses were made before death. Virtual autopsy confirmed 312 (93%) and medical autopsy confirmed 270 (80%) of these diagnoses. In addition to the clinical diagnoses, virtual and medical autopsy together contributed 254 new diagnoses for a total of 590 diagnoses.

Of these 590 diagnoses, 515 (87%) were identified by virtual autopsy, including 73 that were detected solely by postmortem angiography. Fifty-one of these angiographic...
Virtual Autopsy Versus Traditional Medical Autopsy

Original Research

Table 1. New Major Diagnoses Identified by Virtual Autopsy With Multiphase PMCT Angiography and Traditional Medical Autopsy*

<table>
<thead>
<tr>
<th>Case</th>
<th>Age, y</th>
<th>Sex</th>
<th>Underlying Condition</th>
<th>Clinical Cause of Death</th>
<th>New Major Diagnoses and Reasons for Classification</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Virtual Autopsy With Multiphase PMCT Angiography</td>
<td>Traditional Medical Autopsy</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Retroperitoneal hemorrhage†</td>
<td>Retroperitoneal hemorrhage†</td>
</tr>
<tr>
<td>1</td>
<td>78</td>
<td>Female</td>
<td>Pancreatic carcinoma</td>
<td>MI (culprit lesion in the LCA and LAD)†</td>
<td>MI (culprit lesion in the LCA and LAD)†</td>
</tr>
<tr>
<td>2</td>
<td>71</td>
<td>Male</td>
<td>Pneumonia</td>
<td>Septic shock</td>
<td>MI (culprit lesion in the LAD)†</td>
</tr>
<tr>
<td>3</td>
<td>63</td>
<td>Female</td>
<td>Candidemia, liver cirrhosis</td>
<td>Septic shock</td>
<td>Peri-interventional rupture of the SVC‡</td>
</tr>
<tr>
<td>4</td>
<td>77</td>
<td>Male</td>
<td>Aortic valve endocarditis</td>
<td>Septic shock</td>
<td>A: MI (culprit lesion in the LAD)†</td>
</tr>
<tr>
<td>5</td>
<td>74</td>
<td>Female</td>
<td>Pneumonia</td>
<td>Septic shock</td>
<td>MI (culprit lesion in the RCA)§</td>
</tr>
<tr>
<td>6</td>
<td>63</td>
<td>Female</td>
<td>Mitral valve implantation</td>
<td>Cardiac shock</td>
<td>Obstruction of the aortic outflow tract after mitral valve implantation‡</td>
</tr>
<tr>
<td>7</td>
<td>71</td>
<td>Male</td>
<td>Pneumonia (MRSA)</td>
<td>Septic shock</td>
<td>A: MI (culprit lesion in the RCA)†</td>
</tr>
<tr>
<td>8</td>
<td>82</td>
<td>Male</td>
<td>Ischemic cardiomyopathy</td>
<td>Cardiac shock</td>
<td>A: Type B aortic dissection§</td>
</tr>
<tr>
<td>9</td>
<td>62</td>
<td>Male</td>
<td>Non-small-cell lung cancer</td>
<td>Septic shock, cardiac shock</td>
<td>Pleural hemorrhage§</td>
</tr>
<tr>
<td>10</td>
<td>69</td>
<td>Male</td>
<td>Aortic valve endocarditis</td>
<td>Septic shock, cardiac shock</td>
<td>MI (culprit lesion in the RCA)§</td>
</tr>
<tr>
<td>11</td>
<td>82</td>
<td>Male</td>
<td>MI</td>
<td>Cardiac shock</td>
<td>Pneumothorax§</td>
</tr>
<tr>
<td>12</td>
<td>72</td>
<td>Female</td>
<td>Cardiac arrhythmia</td>
<td>Ventricular fibrillation</td>
<td>Esophageal intubation†</td>
</tr>
<tr>
<td>13</td>
<td>53</td>
<td>Male</td>
<td>Cardiac arrhythmia</td>
<td>Ventricular fibrillation</td>
<td>Pleural hemorrhage§</td>
</tr>
</tbody>
</table>

LAD = left anterior descending artery; LCA = left coronary artery; MI = myocardial infarction; MRSA = methicillin-resistant Staphylococcus aureus; PMCT = postmortem computed tomography; RCA = right coronary artery; SVC = superior vena cava.

* In total, 16 new major diagnoses were identified in 13 patients.
† Major comorbid condition not identified before death.
‡ Severe complication of intervention not identified before death.
§ Underlying pathology not identified before death.

New Major and Minor Diagnoses

In addition to the clinical records, virtual and medical autopsy together detected 16 new major and 238 new minor diagnoses. Of the 16 new major diagnoses, 13 were identified by both virtual and medical autopsy. Two new major diagnoses were detected by virtual autopsy alone: tension pneumothorax and esophageal intubation. Almost one half of the diagnoses identified by virtual autopsy (6 of 15) were solely detected by PMCT angiography. One myocardial infarction classified as a new major diagnosis was identified only by medical autopsy (Table 2).

Of the new major diagnoses, all cases of septic shock or pneumonia were identified by physicians, but major hemorrhage (n = 4) and myocardial infarction (n = 4) diagnoses that would have been missed without PMCT angiography were related to cardiovascular diseases, including coronary artery stenosis (n = 32), stenosis of major abdominal or limb arteries (n = 6), and pulmonary embolism (n = 3) as the most important findings.

Medical autopsy identified 474 (80%) of the 590 total diagnoses. Appendix Figure 2 (available at www.annals.org) shows the concordance of virtual autopsy, medical autopsy, and clinical records in identifying diagnoses by proportional Venn diagrams. Table 1 provides more detail and an overview of diagnoses identified by virtual and medical autopsy.

Figure 1. Type B aortic dissection.

Case 8 of Table 2. A. Dissection of the descending aorta identified after multiplephase postmortem computed tomographic angiography; the arrow shows the flap dividing the true from the false vascular lumen (Table 2 [case 8] and Supplement 1). B and C. Histologic section of a longitudinal section through the dorsal wall of the abdominal aorta (original magnification, ×5; each with adapted magnification). Elastica van Gieson stain (panel B) showing dissection zones (1) with 2 interruptions (2a and 2b) and splicing flap from the cranial part of the vessel encountering the outer third of the media, surrounding hyperemic vessels (3), adventitia (4), media (5), fibrous intima (6), and large atheroma with cholesterol crystals (7). Hematoxylin–eosin stain (panel C) showing vital reaction and fresh hemorrhage from vasa vasis into the wall (8).
were identified by autopsy as the cause of death. Aortic dissection (Table 2 [case 8], Figure 1, and Supplement 1), pulmonary embolism (Table 2 [case 5] and Figure 2), and coronary artery stenosis (Table 2 [case 4] and Figure 3) are typical examples of new major diagnoses. Table 2 gives details of all new major diagnoses and explains their classification.

Of the 238 new minor diagnoses, 140 were made by both virtual and medical autopsy, 48 by virtual autopsy alone, and 50 by medical autopsy alone. The largest categories of minor diagnoses were cardiovascular (n = 70) and miscellaneous (n = 84). The largest proportion of new minor diagnoses identified by virtual and medical autopsy was found in the cerebral group (n = 16, representing 64% of all diagnoses in this group). There are also notable differences between virtual and medical autopsy. Virtual autopsy identified only 3 of 7 new minor diagnoses in the group of neoplastic diseases, whereas medical autopsy identified only 1 of 13 fractures and none of the small pneumothoraces (n = 2) in the miscellaneous group.

**Special Aspects: False-Positive Findings and Angiographic Filling Defects**

In many cases, clinical diagnoses of various entities were overruled by 1 or both autopsy methods, labeled as false-positive results, and excluded from the analysis (n = 36). In 11 cases, the radiologist described “unspecific filling defects,” which medical autopsy did not detect.

**DISCUSSION**

Studies on virtual autopsy in the emergency medicine or intensive care setting have shown promising results in many conditions when compared with medical autopsy. However, considerable limitations have been identified for cardiovascular diseases because of cessation of circulation after death (4, 12). In this study of patients who died unexpectedly, the addition of multiphase PMCT angiography to PMCT greatly improved the ability of virtual autopsy not only to confirm antemortem findings but also to identify new diagnoses missed clinically. The addition of PMCT angiography to virtual autopsy detected 73 additional diagnoses; 51 of these were attributed to cardiovascular conditions, including 4 myocardial infarctions classified as new major diagnoses, which highlights the particular benefit of this technique.

The ability to detect cardiovascular conditions is of great importance because cardiovascular events, such as myocardial infarction and pulmonary embolism, are the leading cause of death in most industrialized countries, as in the population investigated in this study (14, 15). Furthermore, in intensive care units, cardiovascular events are the predominant type of new major diagnosis detected retrospectively by autopsy (13). The addition of multiphase PMCT angiography enables clinicians to accurately identify not only substantial hemorrhages but also the hemorrhage site (25). In our study, multiphase PMCT angiography identified 4 hemorrhages classified as new major diagnoses. Regarding the other disease groups, this study confirmed the results of...
our previous study (4) in which we compared virtual autopsy by PMCT without angiography with medical autopsy. As in that study, virtual autopsy and medical autopsy achieved similar results for respiratory diseases and hemorrhages, medical autopsy produced better results for neoplastic disorders, and virtual autopsy performed better for detection of traumatic injuries or findings related to medical devices (Table 2, cases 3 and 12, Figure 5, and Supplement 3). These findings agree with previously published studies (25, 26).

The many new minor diagnoses in the cardiovascular (n = 70) and miscellaneous (n = 84) categories might be explained by the fact that clinicians were often not aware of minor cardiovascular pathologic conditions and the treating physician might not have actively reported minor miscellaneous diagnoses (for example, rib fractures after CPR or small effusions). In addition, that clinicians focus on circulation and ventilation during resuscitation and do not evaluate cerebral findings if these efforts are unsuccessful might explain why cerebral conditions comprise the largest proportion of new minor diagnoses (64% of all diagnoses in this group).

Compared with native PMCT or other angiographic techniques, multiphase PMCT angiography as described by Grabherr and colleagues (20) consists not only of postmortem injection of contrast medium and CT; the addition of the dynamic phase increases the detection of smaller stenoses and hemorrhages. The protocol is highly standardized and has been extensively evaluated in forensic cases.

In a pilot study, Christine and associates (21) investigated multiphase PMCT angiography in 41 forensic cases. They showed that it is less sensitive for detecting parenchymal findings than medical autopsy but detected most pathologic cardiovascular conditions. However, the main limitations of the study are the retrospective analysis of selected cases and inclusion of predominantly trauma patients. Nevertheless, the study supports previously published evidence on postmortem angiography in cardiac disease (27, 28).

The field of virtual autopsy has grown substantially in the past decade, and the use of postmortem angiography is quickly expanding. A MEDLINE search done in November 2013 for “CT AND postmortem angiography” identified about 340 publications; 50% were case reports, and 35 were reviews. Previous studies investigating multiphase PMCT angiography in surgical patients and in a cohort of unselected forensic cases, including patients who died of trauma, intoxication, and natural death related to cancer and cardiovascular diseases, reported promising results for this method (21, 25, 29). Our cohort differed substantially from that of previous studies because we had access to a recent medical history, including diagnostic procedures and standardized emergency department protocols.

Other techniques for postmortem angiography have been established. In a study focusing on 20 patients who died after an event involving chest pain, Ross and coworkers (19) compared medical autopsy with a pump-driven injection of a polyethylene glycol–iopentol solution according to a 2-phase protocol, followed by CT-guided nee-
dle biopsy. They found a strong correlation among virtual autopsy, histologic examination from needle biopsy, and medical autopsy.

Saunders and colleagues (17) reported the use of manual injection of a water-based contrast medium as positive contrast and air as negative contrast for cardiac postmortem angiography in 25 patients. This method is inexpensive and requires almost no preparation, but angiography is restricted to cardiac arteries; it does not detect thromboembolisms, hemorrhages, or infarctions in other organs. In a recent study on 120 cases of sudden death, Roberts and associates (16, 30) showed that targeted postmortem angiography of the coronary arteries is a valuable tool to decrease the number of medical autopsies (16, 30). Unlike in our study, full medical autopsy was done in only 9% of patients and PMCT angiography was limited to the coronary arteries.

We observed some shortcomings of virtual autopsy. First, insufficient mixing of blood and contrast medium in the vascular lumen and postmortem clotting may lead to findings that must be interpreted with caution to avoid false-positive diagnoses of vital occlusions or local stenoses (31). Recognition of this problem is important to prevent misinterpretation, but differentiation based on virtual autopsy alone may be difficult. Insufficient mixing of blood and contrast medium can be identified in real-time angiography by detection of movement of filling defects through the vascular lumen during the scan. Thus, confirming such findings by multiphase PMCT angiography as done in our study is not always possible. The pathologist in our study was not aware of the CT findings and hence focused on the standard medical autopsy and not on confirming the angiographic findings. This may partly explain the many filling defects not confirmed by medical autopsy.

Second, detection of malignant tumors by multiphase PMCT angiography remains difficult and detection of small metastases is almost impossible. Therefore, traditional medical autopsy must still be considered the gold standard for quality control in hematology and oncology. Two studies (32, 33) have evaluated the use of postmortem imaging in combination with guided needle biopsy for histologic examination in unselected patients. However, these studies indicated that virtual autopsy missed cardiovascular diagnoses at a substantial rate. The extent to which virtual autopsy techniques may replace traditional medical autopsy therefore needs further evaluation. Another study (19) evaluated CT-guided needle biopsy after PMCT angiography and was able to achieve results similar to those of traditional medical autopsy in selected patients. However, this study focused on patients who died of acute chest syndromes.

Third, multiphase PMCT angiography requires logistic effort and technical skill in preparing the body by dissecting the vessels and operating the contrast medium pump and CT scanner. The addition of angiography to virtual autopsy increases the cost by about $300 per case for consumables, not including the need for a modified heart–lung machine. Therefore, the economic advantages for virtual autopsies shown in earlier studies are partially offset (33). For targeted angiography of coronary arteries, other techniques may be more feasible (16, 17).

Finally, the high confirmation rate of virtual autopsy in our study may to a certain extent be attributable to the considerable experience of our radiologists in postmortem imaging, whereas the medical autopsies were done within the hospital’s normal routine.

On the basis of our findings, future studies should concentrate on developing techniques that are more cost-effective, require less preparation, and better identify neoplastic diseases. Our study shows that, in cases of unexpected death, the addition of multiphase PMCT angiography substantially improves the value of virtual autopsy, making it a feasible alternative for routine quality control and for identifying diagnoses traditionally made by medical autopsy.

From the University Medical Center Hamburg–Eppendorf, Hamburg, Germany, and Centre Universitaire Romand de Médecine Légale, Centre Hospital Universitaire Vaudois, Lausanne, Switzerland.

Acknowledgment: The authors thank the medical staff of the Department of Intensive Care Medicine for their unfailing commitment to quality control when asking relatives for informed consent to do this study. Furthermore, they thank the technicians of the Department of Legal Medicine for their help in doing the CT scans.

Financial Support: By the University Medical Center Hamburg–Eppendorf. Dr. Grabherr had personal academic funding from the Fondation Lemaîtres. Fumedica provided consumables for multiphase PMCT angiography.

Disclosures: Disclosures can be viewed at www.acponline.org/authors/icmje/ConflictOfInterestForms.do?msNum=M13-2211.

Reproducible Research Statement: Study protocol, statistical code, and data set: Available from Dr. Wichmann (e-mail, d.wichmann@uke.de).

Requests for Single Reprints: Dominic Wichmann, MD, DTM, Department of Intensive Care Medicine, University Medical Center Hamburg–Eppendorf, Martinistrasse 52, D-20246 Hamburg, Germany.

Current author addresses and author contributions are available at www.annals.org.

References
**Current Author Addresses:** Drs. Wichmann and Kluge and Mr. Weinberg: Department of Intensive Care Medicine, University Medical Center Hamburg–Eppendorf, Martinistrasse 52, D-20246 Hamburg, Germany.

Drs. Heinemann, Vogel, and Pueschel: Department of Legal Medicine, University Medical Center Hamburg–Eppendorf, Martinistrasse 52, D-20246 Hamburg, Germany.

Dr. Hoepker: Department of Pathology, University Medical Center Hamburg–Eppendorf, Martinistrasse 52, D-20246 Hamburg, Germany.

Dr. Grabherr: Centre Universitaire Romand de Médecine Légale, Centre Hospital Universitaire Vaudois, Rue du Burgnon 21, CH-1011 Lausanne, Switzerland.

**Author Contributions:** Conception and design: D. Wichmann, A. Heinemann, W.W. Hoepker, K. Pueschel, S. Kluge.

Analysis and interpretation of the data: D. Wichmann, A. Heinemann, H. Vogel, K. Pueschel, S. Kluge.

Drafting of the article: D. Wichmann, S. Grabherr, S. Kluge.

Critical revision of the article for important intellectual content: D. Wichmann, A. Heinemann, H. Vogel, W.W. Hoepker, S. Grabherr, K. Pueschel, S. Kluge.

Final approval of the article: D. Wichmann, A. Heinemann, H. Vogel, W.W. Hoepker, K. Pueschel, S. Kluge.


Statistical expertise: D. Wichmann, S. Kluge.

Obtaining of funding: A. Heinemann, S. Grabherr.

Administrative, technical, or logistic support: D. Wichmann, A. Heinemann, W.W. Hoepker, S. Grabherr, K. Pueschel, S. Kluge.


---

**Appendix Figure 1. Study flow diagram.**

- **Patients with unexplained death**
  - Enrolled ($n = 50$)
  - New major diagnoses ($n = 16$)
  - Postmortem CT angiography only: 2
  - Medical autopsy only: 1
  - Both autopsy methods: 13

- **Excluded ($n = 93$)**
  - Next of kin declined autopsy: 71
  - CT scanner maintenance: 12
  - Funeral scheduled early: 10

- **Next of kin declined autopsy:** 71

- **CT scanner maintenance:** 12

- **Funeral scheduled early:** 10

- **Both autopsy methods:** 140

- **Medical autopsy only:** 50

- **Both autopsy methods:** 140

CT = computed tomography.
Appendix Figure 2. Proportional Venn diagrams for each disease group, showing the concordance of VA, MA, and CR in identifying diagnoses.

Overall (n = 590)

Cardiovascular (n = 191)

Pulmonary (n = 97)

Cerebral (n = 25)

Hemorrhage (n = 36)

Neoplastic (n = 21)

Infectious (n = 30)

Miscellaneous (n = 190)

Values represent the numbers of diagnoses identified by the respective method. Values in overlapping areas of the circles represent the numbers of diagnoses made by the methods sharing in the overlap. For simplification, the labeling is displayed only for overall diagnoses. Diagrams for each disease group are displayed in proportional size to their contribution to the overall diagnoses. Myocardial infarctions or pulmonary embolisms are examples of cardiovascular diseases; pleural effusion or calcification are examples of pulmonary diseases; cerebral hemorrhage or brain infarction are examples of cerebral diseases; infectious endocarditis or pneumonia are examples of infectious diseases; and rib fractures, residual changes after surgery, gallstones, and nephrolithiasis are examples of the miscellaneous conditions. CR = clinical records; MA = medical autopsy; VA = virtual autopsy.