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

A Cohort Study

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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.

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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).

See also:

Web-Only
Supplements

METHODS

Study Design

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

PMCT angiography, with medical autopsy in hospitalized patients who died unexpectedly or within 48 hours of an event necessitating CPR at the University Medical Center Hamburg–Eppendorf, Hamburg, Germany. All eligible cases were reported to the Department of Intensive Care Medicine. In accordance with the requirements of the Ethics Committee of the Hamburg Chamber of Physicians, a physician from the department obtained oral informed consent for virtual and medical autopsy and to use the images in this article. The study was approved by the local clinical institutional review board and complied with the Declaration of Helsinki.

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% Angiofil (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/m^2. 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).

Context

Medical autopsies are being done less frequently and might be replaced by postmortem computed tomography (CT) ("virtual") examinations. Prior studies of virtual autopsies have found deficiencies in the detection of cardiovascular diagnoses.

Contribution

This study found that the addition of angiography to postmortem CT examinations resulted in an ability to detect cardiovascular diagnoses similar to that of traditional medical autopsies.

Caution

Examinations were done at a single expert center.

Implication

Virtual autopsy with CT angiography may be a useful alternative when traditional medical autopsy is not possible.

—The Editors

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

Table 1. **Diagnoses Identified by Clinical Records, Virtual Autopsy With Multiphase PMCT Angiography, and Traditional Medical Autopsy***

Classification of Diagnoses	Clinical Antemortem Records	Virtual Autopsy With Multiphase PMCT Angiography	Traditional Medical Autopsy	Any of the Methods (Cumulative)
Cardiovascular†	114 (60)	176 (92)	179 (94)	191
Pulmonary‡	55 (57)	81 (84)	65 (67)	97
Cerebral§	8 (32)	21 (84)	22 (88)	25
Hemorrhage‖	15 (42)	30 (83)	30 (83)	36
Neoplastic¶	14 (67)	14 (67)	20 (95)	21
Infectious**	26 (87)	25 (83)	29 (97)	30
Miscellaneous††	104 (55)	168 (88)	129 (68)	190
Total	336 (57)	515 (87)	474 (80)	590

PMCT = postmortem computed tomography.
* Values reported are numbers of diagnoses identified by diagnostic method (percentages of the cumulative number of diagnoses made by all methods).
† For example, myocardial infarction and pericardial effusion.
‡ For example, pleural effusion, edema, and pneumothorax.
§ For example, hemorrhagic or nonhemorrhagic stroke.
‖ Other than cerebral.
¶ For example, primary tumors and metastases.
** For example, pneumonia and endocarditis.
†† For example, rib fractures, residual changes after surgery, and nephrolithiasis.

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 euler*APE*, 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

Table 2. **New Major Diagnoses Identified by Virtual Autopsy With Multiphase PMCT Angiography and Traditional Medical Autopsy***

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

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.

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.

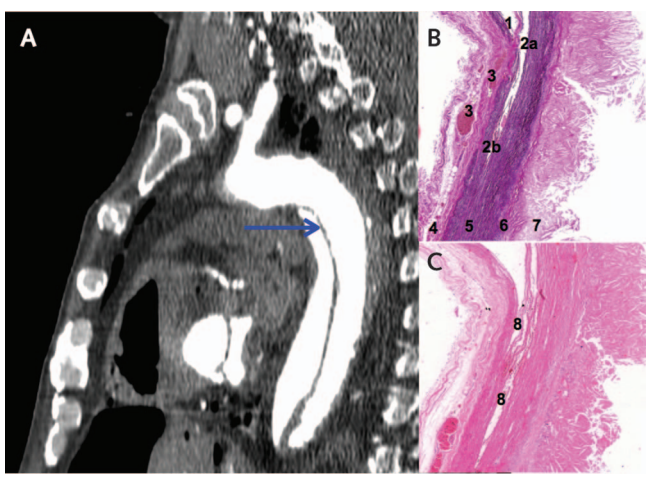
Medical autopsy identified 474 (80%) of the 590 total diagnoses. **Appendix Figure 2** (available at www.annals.org) shows the concordance of virtual autopsy, medical autopsy, and clinical records in identifying diagnoses by proportional Venn diagrams. **Table 1** provides more detail and an overview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

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**).

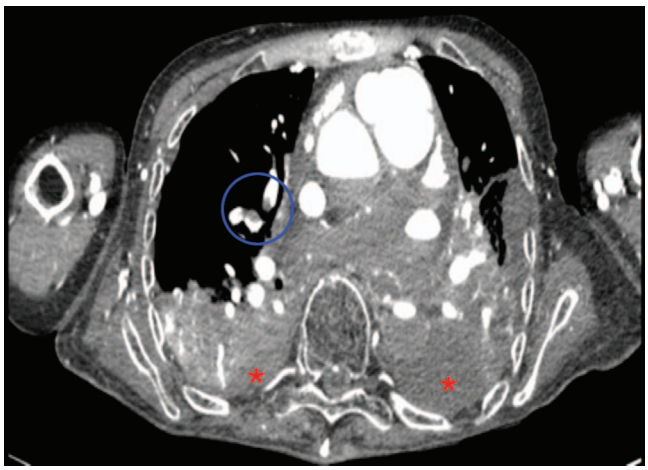
Of the new major diagnoses, all cases of septic shock or pneumonia were identified by physicians, but major hemorrhage ($n = 4$) and myocardial infarction ($n = 4$)

Figure 1. **Type B aortic dissection.**



Case 8 of **Table 2. A.** Dissection of the descending aorta identified after multiphase 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*), fibrotic 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*).

Figure 2. **Pulmonary embolism in the artery of the right upper lobe (*blue circle*), identified by multiphase PMCT angiography.**



Case 5 of **Table 2.** Bilateral fluid accumulation in the dorsal parts of the lung and adjacent pleural space is also shown (*red asterisks*), which probably resulted from postmortem changes due to the 5-day interval between the patient's death and PMCT angiography. PMCT = postmortem computed tomography.

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** (case 9), **Figure 4**, and **Supplement 2** are examples of fatal hemorrhage. **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 pneumothoraxes ($n = 2$) 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.

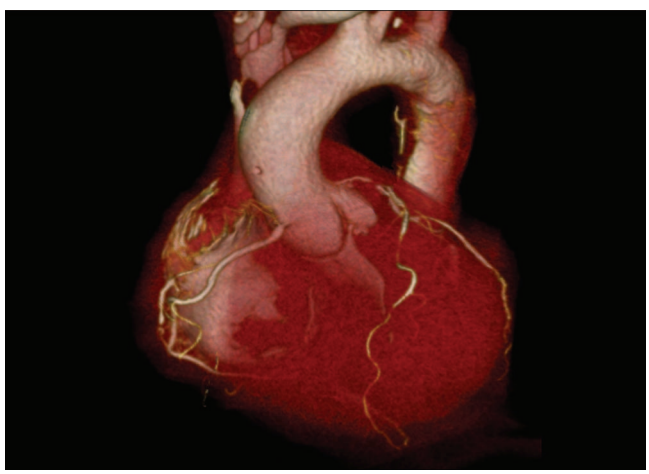
Discussion

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).

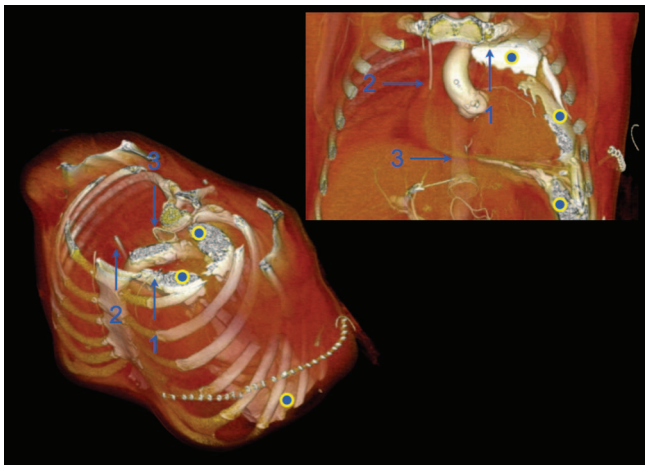
The addition of multiphase PMCT angiography enables clinicians to accurately identify not only substantial hemorrhages but also the hemorrhage site (25). In our study, multiphase PMCT angiography identified 4 hemorrhages classified as new major diagnoses. Regarding the other disease groups, this study confirmed the results of

Figure 3. **Three-dimensional reconstruction of the multiphase PMCT angiography data set showing stenosis of the left descending coronary artery in a patient with fatal myocardial infarction.**



Case 4 of **Table 2**. The angiographic filling distal to the stenosis is a result of collateral filling during the venous and dynamic phases of the contrast medium application. PMCT = postmortem computed tomography.

Figure 4. **Fatal thoracic hemorrhage in a patient who had left-sided pneumonectomy for lung cancer in a 3-dimensional reconstruction of the multiphase PMCT angiography data set in 2 perspectives.**



The hemorrhage, visualized by contrast medium in white and gray (*yellow and blue circles*), was caused by the displacement of a clip (not visible) on a branch of the left internal thoracic artery (*1*) (**Table 2** [case 9] and **Supplement 2**). A central venous catheter (*2*) and Celestin tube inserted into the esophagus because of a bronchioesophageal fistula caused by the tumor (*3*) are shown. PMCT = postmortem computed tomography.

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).

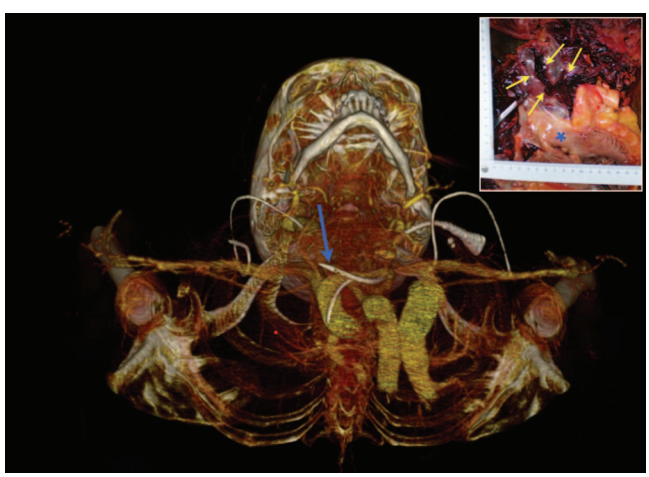
Compared with native PMCT or other angiographic techniques, multiphase PMCT angiography as described by Grabherr and colleagues (20) consists not only of postmortem injection of contrast medium and CT; the addition of the dynamic phase increases the detection of smaller stenoses and hemorrhages. The 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-

Figure 5. **Three-dimensional reconstruction of the multiphase PMCT angiography data set showing perforation of the superior vena cava by a dialysis catheter (*blue arrow*) introduced via the left internal jugular vein.**



Case 3 of **Table 2**. The inset shows the 4-cm-long dissection of the vessel disruption (*yellow arrows*) documented during medical autopsy. The right atrium (*blue asterisk*) is also shown (**Supplement 3**). PMCT = postmortem computed tomography.

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.

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

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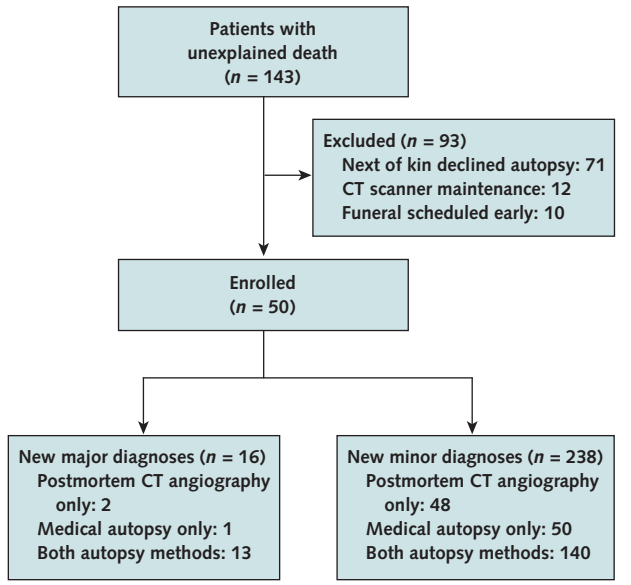
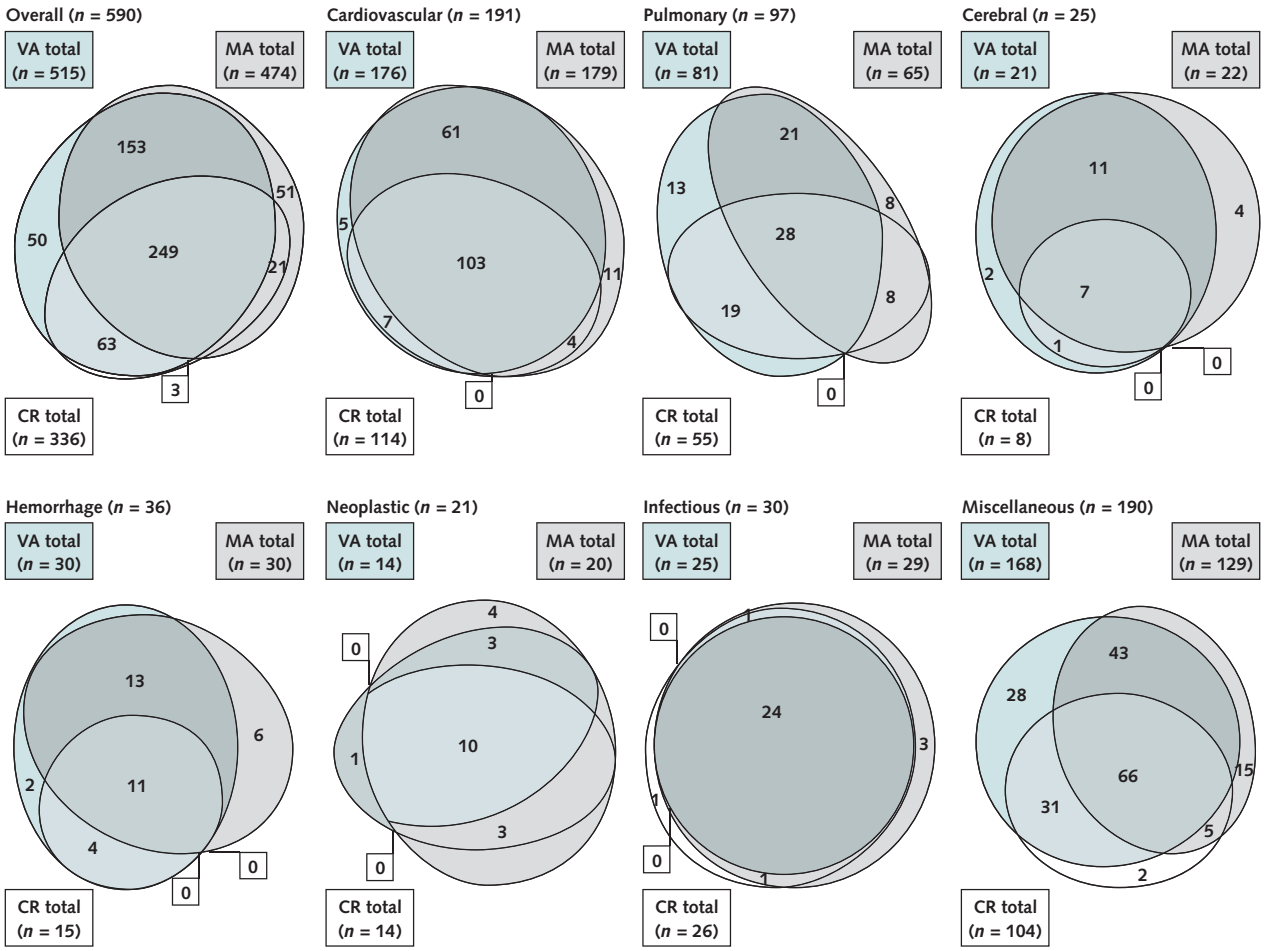
Appendix Figure 1. **Study flow diagram.**



CT = computed tomography.

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



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.