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Insights of Validating Death Certificates through Clinical Autopsies

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Abstract

Background: With decreasing autopsy numbers, the cause of death listed in the death certificate is only based on an external inspection, which is increasingly criticized as insufficient. This investigation analyses 447 death certificates from the archives of the University Hospital of Koeln, Germany and their corresponding autopsy reports from the Institute of Pathology.

Methods: For this analysis, quality assurance protocols, death certificates, clinical/autopsy notes, and final autopsy reports were used. Cases were categorized: 1. in four validation classes (Goldman criteria, identifying unknown diseases with therapeutic relevance as cause of death); 2) in four nosological causal chains (WHO ICD10; type: linear/ divergent/ convergent/ complex).

Results: Differences in diagnoses between death certificate and autopsy report occurred in 32% (143/447 cases). In 7%, only the autopsy identified the cause of death (Goldman, type 2a). Nosological causal chains were established in 21% (linear/divergent) vs 28% (convergent/complex). Myocardial infarct, septicemia and cardiac insufficiency caused death in more than two thirds of cases. Diabetes and obesity did not play a major role as cause of death.

Conclusion: Autopsies are highly advisable if death occurs within 48 hrs. of admission and as sudden death in the hospital setting. Regular interdisciplinary autopsy conferences are important for quality control, assessing cases of the convergent/ complex type. The position of an autopsy commissioner as mediator between relatives, clinicians and pathologists seems recommendable in a hospital setting. While an electronic patient file is still controversial, medical data collection as source of information in emergencies by the patient's medical practitioner seems advantageous.

Keywords: Death certificate; Autopsy report; Goldman criteria; Nosological causal chains; Autopsy commissioner; Electronic patient file.

Introduction

In Germany, about one million people die per year. Board certified medical doctors are oblieged by law to prepare death certificates. Basic diseases, their consequences and a resulting death occuring from a natural event have to be certificed. The massive development in medical knowledge and procedures over the last 30 years and procedures as well as the change in population structure (age increase, ethnicity) has increased the complexity of daily medical practice. In addition, lack of knowledge of the previous medical history of the patient and his preexisting diseases and comorbidites may lead to wrong conclusions. Thus not unexpectedly, during the last decade, the quality of the death certificate and its relation to an autopsy (so called internal body examination) has been increasingly criticized.

To recognize potential problems, the Health Ministry of North Rhine-Westfalia, Germany has suggested to study autopsy-based death certificates versus their respective autopsy reports. Previous analyses focused on particular patient collectives like newborns [1] liver transplantation [2,3], posttraumatic events [19] or intensive care patients [5-7]. An analysis in a community-hospital [8] revealed that a complete agreement between death certificate and autopsy report was only found in 42%. However, a study in a university clinic setting as hospital with all currently available surgical and medical devices regarding the agreement or disagreement between death certificate and autopsy report and its reasons based on nosological causal chains has not been done. We performed this study to

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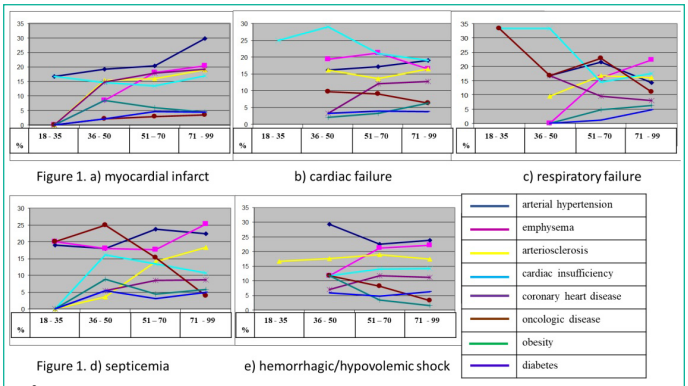

Figure 1. a) myocardial infarct b) cardiac failure c) respiratory failure

Figure 1. d) septicemia e) hemorrhagic/hypovolemic shock

Figure 1:

analyse the reliability on the diagnoses in a death certificate, the need for autopsies based on the recognition of clinical relations, show problematic clinial scenarios and propose ways to improve potential pitfalls.

Material and Methods

Death certificates were validated using clinical autopsies by a team (a board certified anesthesiologist/intensive care specialist (DS) and a board certified pathologist being 20 years head of the autopsy service in the Pathology department of a university hospital). Reports were used from 1420 autopsies performed from 2005 to 2014 at the Institute of Pathology, University hospital of Koeln, Koeln, Germany, one of the largest university hospitals in Germany. Only 447 could be analyzed further due to incomplete/missing clinical information and/or death certificates. Potential diagnostic insights were standardized using case-related quality assurance protocols built on death certificates; applications for autopsy; notes from case discussion between clinicians and pathologists; the autopsy protocol itself and the final autopsy report. This analysis was done in two parts.

Part 1:

Cases were categorized into one of the 4 valuation classes [9] with respect of their role in the cause of death and their diagnoses comparable with those during the life of the patient.

- Class I error: Misdiagnosis that may have affected survival and probably would have required alteration tretatment.
- Class II error: Misdiagnosis that did not affect survival and would not have required alteration of treatment
- Class III and class IV errors: Missed minor diagnoses unrelated to the disease course

Part 2:

Advances in medical knowledge and technology, and the degree of multimorbidity makes the analysis of the cause of death considerably harder than before. As recommended by the WHO, we used the new ICD10 (International Statistical Classification of Diseases and Related Health Problems), where death should be considered the result of a multiple cause chain instead of a single event. In ICD 10, four nosological chains causing death should be used [10,11].

1. Linear type: the classical, monocausal chain (i.e. aspiration – pneumonia – death)

2. Divergent type: a chain whose basic disease is caused/characterized by two different disease processes (i.e. diabetes: macro- / microangiopathy; nerve paralysis and “diabetic foot” etc.).

3. Convergent type: a causal chain with a common final denominator (e.g. hypertension/diabetes/fatty acid disturbance: all causing microangiopathy leading potentially to cardiac infarction).

4. Complex type: several parallel existing diseases with an independent and equally strong contribution leading to death (e.g. inflammatory bowel disease and prostatic abscess both leading to septicemia).

5. All cases were subjected to nosological causal chain evaluation.

The following statistical analyses were performed:

i. Quality assurance protocols were established quantifying the diagnostic gain using autopsies by differentiating the relationship between basic/essential versus secondary illnesses

ii. Frequency distribution of valuation classes (according to Goldman; methods, part 1)

iii. Frequency of nosological causal chains

Results

Patient Data

We analyzed death certificates and autopsy reports from 447 patients, 192 men (43%) and 255 women (57%) (age distribution see Table 1). Patients came from either the university clinic (353; “inpatients”) or as outpatients/emergency cases (94) (see Table 2). The majority in both groups constituted patients from

Table 1: Age and gender distribution.

Age	Number of patients	in %	males	in %	females	in %	M : F
18 – 35	21	4.7	8	3.1	12	6.3	1.8 : 2.7
36 - 50	75	16.8	44	17.2	29	15.0	9.8 : 6.5
51 - 70	212	47.4	133	52.2	80	41.7	29.8 : 17.9
71 - 99	139	31.1	70	27.5	71	37.0	31.3 : 31.7
			255	100.0	192	100.0	447 = 100.0
Gender							
M	192	43.0					
F	255	57.0					
	447	100.0					

Table 2: Patient recruitment.

	Primary patient from university clinic (“inpatients”)		Patient transfered as emergency case (“outpatients”)	
Medical discpline/Institute	total #	in %	total #	in %
Kardiology	157	44,4	47	50.0
Gastroenterology	79	22.3		
Oncology	53	14.7		
Gerneral surgery	43	12.1	39	41.5
Vascular surgery			4	4.2
Orthopedics	3	0.8		
Other surgical disciplines	6	1.7		
Neurology	12	3.4	4	4.2
Total number of all cases	353	100	94	100

cardiology (inpatients: 44.4 vs emergency patients: 50%) and the GI department (inpatients: 22.3%). General surgery patients were dominant as emergency patients (41.5% vs. 12.1% as inpatients); patients from oncology were the next largest group for inpatients (14.7%). A more detailed differentiation was not possible in the emergency cases.

Emergency Diagnoses

Patients were delivered as emergency cases from their homes/outside hospitals with a variety of serious different symptom / suspected diseases, of which circulatory arrest and myocardial infarct were the most frequent ones (representing more than 20% of all cases) followed by dyspnea, thorax pain and arrhythmias (Table 3).

The Compilation of Diseases from Inpatients

Cardiac diseases such as myocardial infarct (41.8%) and cardiac insufficiency/cardiomyopathy (21.2) represent about two thirds of all cases, followed by liver (39.3%), renal diseases (22.6) and gastrointestinal bleedings (4.4%) (Table 4). There were no significant gender difference between respective major diseases.

Major Basic Diseases

Major basic diseases from autopsy reports were arterial hypertension, pulmonary emphysema well as other cardiac diseases (Table 5) Oncologic diseases/immunosuppression with 8.7 percent were less prominent.

Table 3: Emergency diagnoses.

Emergency diagnoses	sum #	in percent
circulation arrest of unknown cause	30	22.2
myocardial infarct	28	20.7
dyspnea	17	12.6
thorax pain	16	11.9
arrhythmia	12	8.9
neurologic deficits/syncope	12	8.9
hypotension	8	5.9
others	12	8.9
total		100

Table 4: Diseases of various organs.

Diseases of various organ systems	Sum #	in percent
myocardial infarct	148	22.4
liver failure/- diseases	139	21.1
renal failure/ - diseases	80	12.2
cardiac insufficiency/ cardiomyopathy	75	11.4
gastrointestinal bleeding	51	7.8
pulmonary edema/ lung bleeding	42	6.6
diverticulosis/ diverticulitis	38	5.7
pancreatitis	37	5.5
metastases	27	4.1
Others	21	3.1
all organ systems	658	100

Table 5: Diseases confirmed by autopsy (multireferencing).

Diseases confirmed by autopsy (multireferencing)	sum #	in percent
arterial hypertension	216	14.9
pulmonary emphysema	190	13.1
arteriosclerosis	130	8.9
Coronary heart disease	117	8.0
Cor pulmonale	104	7.2
cardiac insufficiency/cardiomyopathy	85	5.8
myo-/endo-/pericarditis	75	5.2
pneumonia	74	5.1
other inflammatory diseases	162	11.1
leukema/immunosuppression	126	8.7
others	175	12.0
total # of diseases	1454	100.0

There were no significant gender difference between respective major disease; arterial hypertension and pulmonary emphysema being slightly more frequent in female ´than in male patients (Table 6).

Nosological Causal Chains

Cases categorized in nosological causal chains show an equal distribution for the linear/ divergent type in 21% versus 28.5% for the convergent/ complex type (Table 7).

Cause of Death

Causes of death were evaluated as described in autopsy reports. Among the five most frequent causes we found cardiac/circulatory failure (29.8%), septicemia (21.6%), myocardial infarct (18.8%), respiratory failure (5.9%), and hemorrhagic shock/aortic dissection (4.2%). Others were less frequent (Table 8).

According to age of death (Table 9), we observed in the young adult (age 18 – 35), death due to bleeding was the most prominent followed by cardiac failure. With increasing age, myocardial infarction became the most dominant cause of death (34% aged group 51 – 70; 32.7% in age group 71 – 99). The second most drominent cause was septicemia, even outnumbering myocardial infarction particularly in the 36 – 50year old patients.

Table 6: Major basic diseases in males/females (multireferencing).

major basic diseases	male patients		female patients	
	sum #	in percent	sum #	in percent
arterial hypertension	138	21.7	113	23.5
pulmonary emphysema	131	20.5	110	22.9
arteriosclerosis	108	17.0	71	14.8
coronary heart disease	84	13.2	60	12.5
cardiac insufficiency	110	17.3	81	16.9
Oncologic disease	66	10.3	45	9.4
Total # of diseases	637	100	480	100

Table 7: Nosological causal chains.

Nosological causal chain	# of patients	In %
Type 1: linear	95	21.2
Type 2: divergent	97	21.7
Type 3: convergent	128	28.6
Type 4: complex	127	28.5
Total #	447	100

Table 8: Causes of death according to autopsy reports.

Cause of death according to autopsy reports(inpatients)	In percent
cardiac/circulatory failure	29.8
septicemia	21.6
myocardial infarct	18.8
respiratory failure	5.9
hemorrhagic shock/aortic dissection	4.2
left heart failure	4.0
right heart failure	2.6
lung arterial embolism	3.6
gastrointestinal bleeding	2.8
myo-/ endo-/ pericarditis	1.8
pneumonia	1.5
others	3.8
Total number of cases: 354	100.0

Significant differences in the frequency of basic diseases (arterial hypertension, emphysema, arteriosclerosis, cardiac insufficiency, coronary heart disease, oncologic diseases, obesity, diabetes) as potential forerunners of the 5 most prominent causes of death were identified (Table 8) at different age groups (Figure 1). For inpatients, in 70% a heart/circulation failure, septicemia or a myocardial infarct was the cause of death. For myocardial infarct as cause of death, arterial hypertension, arteriosclerosis, cardia insufficiency and the degree of pulmonary emphysema showed an increasing importance over age (Figure 1a). Similarly, the same factors affected the death of cardiac failure (Figure 1b). In respiratory failure, the amount of pulmonary emphysema was most prevalent with a stepwise increase from 36 to 99 years of age. In the youngest age group respiratory failure was predominantly caused by pneumonia (Figure 1c). Death due to septicemia was influenced by arterial hypertension and arteriosclerosis (Figure 1d); the pulmonary function also playing a major role. Oncologic diseases were dominating in the age group 36 – 50 years as forerunners of septicemia. In later age groups, oncologic diseases play only a minor role, while arteriosclerosis is rising. All other disease entities were of minor importance (less than 10%). In case of bleeding (Figure 1e) the arterial pressure and the degree of arteriosclerosis were most important (>20%). Oncologic diseases played a prominent role in pulmonary failure and in septicemia in the younger age groups. In contrast, obesity and diabetes were only of minor importance. In summary, with increasing age, myocardial infarct, respiratory failure and septicemia are rising and comprise about two thirds of all deaths.

Discrepancy between Causes of Death in Death Certificates vs. Autopsy Reports

The analysis between the cause of death on a death certificate versus the respective information on the autopsy report showed an agreement in 68% overall (304/447 cases). In 32%, however, the diagnoses between the two documents did not match (143/447) (Table 10) Myocardial infarct (36/143; 25.1%) and septicemia (28/143; 19.6%) were the most commonly misdiagnosed, occurring concurrently in 3.5% (5/143). At third place, hemorrhagic/hypovolemic shock due to bleeding (19/143; 13.3%) was misinterpreted. Pulmonary embolism was unrecognized in 6.3% (9/143). In 10/143 misdiagnosed cases (7%), the autopsy was essential in detecting the cause of death; the death certificates listed here as cause unknown/unclear/none.

Table 9: Causes of death (primary inpatients and outpatients/emergencies from outside).

	18 - 35	in %	36 - 50	in %	51 - 70	in %	71 - 99	In %
myocardial infarct	3	14.3	19	22.3	60	34.1	54	32.7
septicemia	3	14.3	36	42.4	39	22.2	38	23.0
cardiac failure	5	23.8	17	20.0	28	15.9	26	15.8
hemorrhagic shock/hypotension	6	28.6	8	9.4	22	12.5	21	12.7
respiratory failure	4	19	5	5.9	27	15.3	26	15.8
total # of cases: 447	21	100.0	85	100	176	100	165	100

Valuation by Goldman Criteria

Our data show a class I error in 32% (Table 10). These cases show the same frequency distribution in type 1 and 2 nosological causal chains. The frequency of the convergent type is with 34.3% slightly higher; the type 4 is unexpectedly slightly less frequent (23.9%) compared to the overall number of cases (28.5%) (Table 11 vs.7).

Discussion

The analysis of 447 death certificates plus autopsy reports showed that cases belonged in 21% to type 1 and 2 nosological causal chains and in about 28% to type 3 and 4. We found an overall discrepancy in the cause of death between death certificate and autopsy report in 32%. We experienced difficulties to posthumously differentiate in major errors (clinically missed diagnoses involving a primary cause of death) versus class I errors (likely to have affected patient outcome), because several cases being part of either category. Thus, we combined these cases as class I errors (misdiagnosis that may have affected survival and probably would have required alteration of treatment) [12]. Wiitekind and Gradistanac (2018) have reported frequencies of such errors ranging from 2.4 to 19%. Shojania et al. (2003) analysed 53 autopsy-series and calculated 23.5% (range, 4.1%-49.8%) for major errors and 9.0% (range, 0%-20.7%) for class I errors, being in the same total range of 32% of our study.

Decreasing Autopsy Numbers and Its Possible Causes

The concern raised by the North Rhine Westfalia Ministry of Health regarding the major discrepancy between cause of death in death certificates and in autopsy reports seems to be justified not only for regional hospital [8] But also at the university level (discrepancy 32%). This problem is most likely caused by the dwindling numbers of autopsy performed at the university hospital, where a decline of autopsy numbers of 58% is reported from 1993 to 2014 [14]. The problem is, however, widespread: already in 2008, Tavora et al. reported from the United States a major discrepancy involving the cause of death in 17.2% (50 cases) analyzing autopsy records from three institutional settings. Various other publications over the past decades have pointed to decreasing autopsy numbers and the subsequent lack of quality control of clinical measure [13,16,17,19]. This decrease has been made responsible for the substantial number of incorrect diagnoses on death certificates [18]. Winter et al (2012) reported up to 40.500 cases of misdiagnoses per year particularly in the Intensive Care Units (ICUs). Even in the era of "high-tech" medicine, autopsies have detected previously unknown causes of death [19]. In the literature, this discrepancy occurred in 8.4 to 24.4% [13], while from some university hospitals still relatively high autopsy numbers are reported (median 6.1%; mean 2.4%; Nemetz et al., 2006). This is not the case in the vast majority of non-academic hospitals where only a few or no autopsies at all are performed. This decrease is regarded as a negative effect for medical education and quality of care in a yet unprecedented scale [21]. This may already be reflected in the study of Betz et al (2008) from the Beth Israel Hospital in Boston. They conducted an anonymous Web-based test, questioning MDs regarding prior training and experience in completion of death certificates. In contrast to the clinicians' high level of confidence in their ability to complete a death certificate accurately, only 52% filled out the death certificate with the correct primary cause of death and 10% listed the three major contributing causes of death. However, the use of autopsies for educational purposes is evaluated with regional differences: residents

Table 10: Discrepancy of cause of death between autopsy report and death certificate.

Case #	cause of death by autopsy	cause of death by death certificate
1	aortic dissection	cardiac/circulatory failure, septicemia
	arrythmia	none
	brain stem compression	respiratory insuffciency
	cardiac insufficiency	myocarditis, pulmonary embolism, myocardial infarct
5	cardiac insufficiency	septicemia
	cardiac metatsases, failure	pneumonia, lung metatsases
	cardiac tamponade	pulmonary embolism
	cardiac/circulatory arrest/ arrhythmia	septicemia
	cardiac/circulatory arrest / arrhythmia	unclear
10	cardiac/circulatory arrest / arrhythmia	unclear
	cardiac/circulatory arrest/ arrhythmia	myocardial infarct
	cardiac/circulatory arrest/ arrhythmia	respiratory insufficiency
	cardiac/circulatory arrest / arrhythmia	thyreotxoic crisis
	cardiac/circulatory arrest / arrhythmia	aspiration, septicemia
15	cardiac/circulatory arrest / arrhythmia	myocardial infarct
	cardiac/circulatory arrest/ arrhythmia, intracerebral bleeding	septicemia, intestinal ischemia
	circulatory failure	septicemia
	endocarditis	pulmonary edema
	endocarditis	right heart failure
20	endocarditis	electromechanical decoupling, cardiac failure
	endocarditis, moycardial infart	unknown
	fungal septicemia	meningitis
	gastrointestinal bleeding, hypovolemic shock	liver failure, multiple organ failure
	gastrointestinal bleeding, hypovolemic shock	septicemia, circulatory failure
25	gastrointestinal bleeding	multiple organ failure
	hemorhagic shock, respiratory insufficiency	cardiac/circulatory arrest/ arrhythmia, septicemia
	hemorrhagic shock	pneumonia, right heart failure
	hemorrhagic shock	liver failure
	hemorrhagic shock	electromechanical decoupling
30	hemorrhagic shock	aspiration
	hemorrhagic shock	septicemia, pneumonia
	hemorrhagic shock	respiratory failure
	Hemorrhagic shock	septicemia
	hemorrhagic shock	myocardial infarct
35	hemorrhagic shock, aortic rupture	pulmonary embolism, cardiac failure
	hemorrhagic shock, myocardial infarct	electromechanical decoupling
	hemorrhagic shock, myocardial infarct	electromechanical decoupling
	hemorrhagic shock, myocardial infarct	septicemia
	hemorrhagic shock, myocardial infarct	liver failure
40	hemorrhagic shock, myocardial infarct	septicemia
	hemorrhagic shock, myocardial infract	cardiogenic shock
	hypovolemic shock	arrythmia, upper gastrointestinal bleeding
	hypovolemic shock/ myocardial infarct	septicemia
	hypovolemic sock	septicemia
45	left heart failure	intestinal ischemia, liver failure
	left heart failure	unknown
	left heart failure	septicemia, multiple organ failure
	left heart failure	anphylaxia, unclear
	left heart insufficiency	septicemia, multiple organ failure
50	liver failure	aspiration
	liver failure, septicemia	brain edema, bleeding
	metabolic /toxic circulatory failure	paralytic ileus
	metabolic/ toxic circulatory failure	unclear
	metabolic/ toxic circulatroy failure	lymphoma
55	myocardial infacrt	cardiac/circulatory arrest caused by bleeding
	myocardial infacrt	right heart failure
	myocardial infarct	cardiopulmonal decompensation
	myocardial infarct	septicemia
	myocardial infarct	pulmonary embolism
60	myocardial infarct	intestinal ischemia
	myocardial infarct	unknown, multiple organ failure
	myocardial infarct	septicemia, multiple organ failure
	myocardial infarct	right heart failure
	myocardial infarct	pulmonary embolism, aortic rupture
65	myocardial infarct	endocarditis
	myocardial infarct	right heart failure
	myocardial infarct	cardiac failure, electromechanical decoupling
	myocardial infarct	septicemia, acute abdomen
	myocardial infarct	septicemia, cardiac shock
70	myocardial infarct	septicemia, pneumonia

	myocardial infarct	left heart failure
	myocardial infarct	pulmonary embolism, cardiac/circulatory arrest / arrhythmia
	myocardial infarct	pulmonary embolism, electromechanical decoupling
	myocardial infarct	hypotonia, metabolic acidosis
75	myocardial infarct	septicemia
	myocardial infarct	cardiac failure , cardiac insufficiency
	myocardial infarct	electromechanical decoupling
	myocardial infarct	septicemia
	myocardial infarct	hemorrhagic shock
80	myocardial infarct	pneumonia
	myocardial infarct	hemorrhagic shock
	myocardial infarct	myocarditis
	myocardial infarct	cardiac/circulatory failure
	myocardial infarct	cardiac/circulatory arrest / arrhythmia
85	myocardial infarct	septicemia, rhabdomyolysis
	myocardial infarct	cardiac/circulatory arrest /arrhythmia
	myocardial infarct	septicemia
	myocardial infarct, aortic dissection, hemorrhagic shock	septicemia
	myocardial infarct, left heart failure	septicemia
90	myocardial infarct, myocardial bleeding	none
	myocarditis	unclear
	pericardial tamponade	pericardial effusion
	peritonitis, septicemia	liver failure, postop cardiac shock
	pneumonia	electromechanical decoupling
95	pneumonia	pulmonary bleeding, hypoxia
	pneumonia	electromechanical decoupling
	pneumonia	intracerebral bleeding
	pulmonary embolism	cardiac shock
	pulmonary embolism	myocardial infarct
100	pulmonary embolism	electromechanical decoupling
	pulmonary embolism	endocarditis
	pulmonary embolism	unclear
	pulmonary embolism	intracerebral bleeding
	pulmonary embolism	intestinal ischemia, acute abdomen
105	pulmonary embolism	cardiac failure
	pulmonary embolism	herniation
	respiratory insufficiency	pneumonia
	respiratory insufficiency	none
	respiratory insufficiency, stroke	pulmonary embolism
110	respiratory insuficieny, right heart failure	brain edema, encephalitis
	right heart failure	myocardial infarct
	septicemia	intestinal ischemia, disseminated intravascular coagulation
	septicemia	pneumonia
	septicemia	aspiration
115	septicemia	aspiration, ileus
	septicemia	multiple organ failure
	septicemia	right heart insufficiency, liver failure
	septicemia	respiratory insufficiency
	septicemia	left heart insufficiency
120	septicemia	respiratory insufficiency
	septicemia	pneumonia, aspiration
	septicemia	intestinal perforation
	septicemia	bilateral pulmonary embolism
	septicemia	herniation, brain edema
125	septicemia	electromechanical decouling, respiratory insufficiency
	septicemia	sudden cardiac death, arrythmia
	septicemia	intestinal ischemia
	septicemia	respiratory insufficinecy
	septicemia	respiratory insufficiency, acute respiratory distress syndrome
130	septicemia	liver failure
	septicemia	gastrointestinal bleeding
	septicemia	cardiac failure
	septicemia	hemorrhagic shock, cardiac failure
	septicemia	amyloidosis
135	septicemia, myocardial infarct	respiratory insufficiency, aspiration
	septicemia, myocardial infarct	pulmonary embolism
	septicemia, myocardial infarct	septicemia
	septicemia, myocardial infarct	septicemia
	septicmeia, myocardial infarct	cardiac/circulatory arrest /arrhythmia
140	sudden cardiac death	septicemia, intestinal ischemia
	thrombophlebitis	paralytic ileus
	toxic cardiac/circulatory failure	septicemia
	toxic cardiac/circulatory failure, respiratory failure	cardiac failure

Table 11: Nosological causal chains in discrepant diagnoses between death certifictaes and autopsy reports vs total number of cases in each category.

Nosological causal chain	# of patients	In %
Type 1: linear	28/ 95	19.5/ 21.2
Type 2: divergent	31/ 97	21.6/ 21.7
Type 3: convergent	49/128	34.3/ 28.6
Type 4: complex	35/127	23.9/ 28.5
Total #	143/447	32.0/ 100.0

in pathology and internal medicine working at the Massachusetts General Hospital being associated with the Harvard Medical School as teaching hospital positively reflected the value of autopsies for educational purposes, to answer open clinical questions and as source for scientific research [21].

What are the Measures Being Recommended/Taken to prevent this Trend?

In 2017, the German Society of Pathology [14] renewed its guidelines recommending scenarios in which an autopsy should be considered. The major guidelines concerning the recommendation for autopsies in cases of death of adults with regard to our study in a university hospital are the following four:

i. Unexpected death in a hospital setting/ death from non-plausible causes

ii. Death occurring within 48hrs after hospitalization

iii. Post-/perioperative death following invasive procedures (ev. after release by prosecuting attorney's office)

iv. death in the context of a suggested occupational disease

In the following paragraph, we will briefly discuss relevant cases to highlight these four recommendation and name potential problems.

Unexpected Death in a Hospital Setting/ Death from Non-Plausible Causes

Case 1: One of the most problematic causes of death is a pulmonary embolism [12]. We could observe this scenario in a variety of oncology patients with different tumors such as vein thrombosis following bladder carcinoma; prostate cancer with massive thrombi formation in the periprostatic veins, pancreatic and prostate cancer causing ascending leg vein thrombosis, all of which were followed by a fatal pulmonary embolism. In almost all cases the cause of death (before autopsy) given on the death certificate was myocardial infarct.

Case 2: A patient was diagnosed with a Coronavirus infection during his stay in the hospital but seemed otherwise unaffected in the previous afternoon. In the evening hours, he got up, collapsed and fell, breaking his cheek bone. He was found the next morning, successfully operated but experienced a progressive septicemia leading to his death about 24 hrs. after the incident. Since these events occurred in a hospital setting, he was autopsied by a pathologist, revealing as signs of death small peripheral lung emboli, bleeding and septicemia fitting the diagnosis of a Corona virus induced septicemia.

Death Occurring within 48hrs after Hospitalization

In case of a sudden death within 48 hours of delivery into a hospital an autopsy is highly recommended, particularly if this happens on a weekend. In most cases, any laboratory investigation will not yet be completed; radiologic investigations are not yet performed. The cause of death is solely depending on the limited information, which accompanied the patient (e.g. reports, patent file). Since death occurs so suddenly, relatives are often concerned that not everything possible was done for the patient, which admittedly may be true regarding the insufficient time for any investigation. Thus, an autopsy may help the relatives to understand the course of the disease and the final demise at this time.

As exemplary case we present a 30 year old male who has been imprisoned in Eriwan, at the time part of the Russian federation, where he got infected with tuberculosis. He was treated with a tuberculostatic monotherapy only. After his release, he traveled to Rome, from there to Paris and finally by train to Cologne, Germany, where he collapsed at the train station. Hospitalized as emergency in the university hospital, a renal insufficiency was noted. The patient died less than 48 hrs. after admission. At autopsy, a massive tuberculoid necrosis of his left psoas muscle extending to the inguinal ligament was found. No other site or lymph nodes were positive for Tbc.

Both kidneys showed histologically and immune histologically an AA amyloidosis as cause of his renal insufficiency. The autopsy result was cause of great concern to the respective Italian/French and German authorities; however, no infectious spread was ever reported.

Post-/Perioperative Death Following Invasive Procedures (Ev. After Release by Prosecuting Attorney's Office)

Patent's death following an intervention is often expected to be a case for forensic pathology; occasionally, the prosecuting attorney's office will release the body for autopsy at the Pathology department. However, in our experience, most often the underlying cause is not negligence but rather an unknown or prior undetectable anatomic malformation. In one of those cases, the catheterization of the right coronary artery lead to a dissection with a major intramural myocardial bleed which got infected leading to a combination of infarct plus myocarditis affecting the atrium and the major parts of the right ventricle. This condition ultimately caused myocardial death. The dissection was caused by an extremely narrow opening into the right coronary artery from the aorta.

In TAVI procedures, the success can be hampered by the high degree of valve calcification of the aortic cusps as well as complications following an unrecognized endocarditis [23].

Death in the Context of a Suggested Occupational Disease

Occupational diseases such as pneumoconiosis can be autopsied by request from the relatives, since compensations are in order if the pulmonary disease played a substantial role in causing death. However, there is often a difference in the clinical appearance (lung function) and the detectable degree of structural damage. Occasionally, the development of tuberculosis, or even a pleural mesothelioma are suspected, which are considered a major cause of deterioration of the occupational disease. However, an autopsy is mandatory since such a course cannot be considered on clinical/radiologic means only. Mesotheliomas are potentially difficult to diagnose due to the mantel-like fibrosis encasing the lung lobe. However, more often than not the patient has another underlying disease: malignant neoplasms of the lung as well as other organs (skin, pancreas, prostate or kidney) can mimic pleural mesothelioma and if so, are defined as 'pseudo-mesothelioma'. Saleh et al. (2021) de-

scribed in a study of 8 autopsy cases for occupational disease 3 cases of malignancy due to pulmonary adenocarcinoma, and one of squamous cell carcinoma originating from the diseased lung. All of which are not recognized as pathophysiologic disease related to a compensated occupational hazard. A bizarre case even revealed a papillary renal cell carcinoma metastasizing into the pleural cavity.

In spite of these recommendations, there seems to be a lack of willingness to ask for and perform an autopsy. This has several reasons.

Autopsy Consent Depends on Patient's Relatives and Attitude of the Treating Physicians

Autopsy consent is multifactorial [20] and depends on patient's relatives as well as the treating physicians in the case. The communication between the relatives and the former treating physicians is of the essence [18,25]. A strong recommendation for an autopsy will clearly increase the likelihood of a consent from the relatives [18]. Further reasons for relatives to refuse an autopsy request as listed by medical staff from pathology and internal medicine varied considerably (discomfort; cause of death "is already known"; confusion about the actual procedure; autopsy considered disrespectful behavior; disturbance of the peace of the dead; religious/morale reasons) [21]. In contrast, Tsitsikas et al (2011) reported that the public was in favor of an autopsy as long as results were presented honestly and in detail as well as open information about the autopsy procedure itself (e.g. organ analysis; tissue preservation and examination).

Objections to an autopsy from the medical staff are primarily economical in nature [20] as well as the erroneous belief that the progressing medical diagnostics and effective therapy would reduce the value of an autopsy to such a minimum of new information, that it is not worth while risking an autopsy injury with contraction of an infectious disease (e.g. particularly hepatitis B and C, tuberculosis; HIV). In addition, the work load is intensive, and an autopsy binds experienced staff, which represents an unattractive monetary situation for a hospital [20,26]. On the other hand, in a Norwegian study of 250 general practitioners and clinical doctors, 42% voiced a positive opinion about the value of an autopsy in spite of medical advancements in diagnostic procedures and therapy [27].

Full Body Autopsy Alternatives only in Exceptional Cases

Alternative procedures have been assessed as potential replacement for a full body autopsy such as minimal invasive investigations (needle biopsies; endoscopy) as well as different radiologic techniques. While these procedure may appeal to relatives being less "aggressive", they are much less accurate than the autopsy in gaining information and sampling of tissues samples, while they need specially trained personnel and equipment leading to increasing costs [18].

However, the option of an autopsy limited to a specific organ/organs may suffice. A sudden and unexpected death in a 5 year old girl occurred, who had experienced previous signs of upper respiratory infection. A myocarditis was suspected. Since the parents were strongly opposing a full body autopsy, heart muscle tissue was taken (from an autopsy limited to the heart), in which molecular analysis identified a Parvo virus myocarditis.

In another case of an elderly woman suffering from liver failure, a full body autopsy was refused by the relatives. A liver-only autopsy was agreed which showed massive liver metastases. To reveal the source of this previously unknown tumor, immune histologic analysis was done, which showed markers in accordance with a papillary serous carcinoma of the ovary.

The Problem of Time for the Post-Mortem Examination

Delaying an autopsy for more than 24 hrs. after death may well lead to difficulties in the evaluation of the diagnoses listed on the death certificate, particularly if premortal diseases are suspected leading to an accelerated decay of body tissues (such as septicemia, chemotherapy, hematologic diseases; post bone marrow transplant; as well as no suitable cooling chamber for preservation of the body).

A critical time factor arises in an autopsy which has been primarily directed to forensics, of which organ parts are subsequently sent to pathology for detailed evaluation. If there is insufficient material being preserved by fixation or there is a prolonged time period between time of death and this subsequent analysis (which often happens due to the administrative / judicial course of events) materials may be no longer preserved well enough for molecular analysis, as exemplified in the following case.

After a tonsillectomy, a 30 year old female bled so profusely, that in spite of surgical intervention by ligation of neck arteries, the patient died. The surgeon being accused of negligence, called for a forensic autopsy. Since specialized histologic analyses were needed; pathology was involved, showing a unique malformation of superior neck arterioles (segmental mediolysis). The value of this autopsy lies in the exculpation of the operating surgeon from the initial accusation. However, the attempt of a molecular analysis of this conatal condition, was thwarted due to the degradation of the RNA, which would have been necessary for further analysis [28].

A Good Relationship to Forensic Pathology is Mandatory for Achieving Best Results in Autopsy Cases

A well working interaction between pathology and forensic medicine is very beneficial and important. Histological/immune histological/ molecular aspects can be of an asset for pathology to aide the forensic analysis. On the other hand, there are cases in which the cause of death is appears highly likely resulting from wrongdoing so that the autopsy should be stopped and continued by the forensic pathologist. As exemplary case we observed a 28 year old male with a history of recurrent pneumonias and pleural effusions. The patient returned to an outside hospital with a massive pleural effusion which needed to be drained. During the night the puncture site bled internally clinically unnoticed, and he died the same night. A regular pathology autopsy was performed unbeknown of the exact medical history (as death following recurrent pneumonia) (lack of clinical data from an outside hospital). Opening the pleura on the former puncture site, a massive hemothorax was discovered. At that point, the autopsy was transferred to the forensic department for specific analysis. The result showed several adhesions, which were undetectable by X-ray following the massive effusion. Fatefully, the treating physician happened to puncture through one of them leading to the deadly bleeding.

Improving Communications is Crucial for Autopsy Permission: the Autopsy Commissioner

To overcome relatives' arguments of an autopsy rejection it seems evident from the above discussion that an improved communication is imperative. This involves training physicians

to favor an autopsy, sufficient time without time pressure and an environment (special room, furniture setting, flowers, pictures, etc.) which is conducive for such a difficult topic to discuss. In our opinion for the university /larger hopsitals, an autopsy commissioner, being a highly qualified (board certified) and experienced (older) clinician could be an ideal mediator to assess and discuss the case with the treating clinicians involved as well as acting as an understanding partner for the relatives. He should also be well aware of the applying legal situation, and be able to competently interact with the funeral director/ staff.

Interdisciplinary Autopsy Conferences Based on Quality Assurance Protocols and Autopsy Reports

The understanding for the need of autopsies can be greatly improved when regular interdisciplinary autopsy conferences are part of the weekly clinical curriculum and will be of great help in teaching students. Hereby, quality assurance protocols and autopsy reports as well as a review of the discussed case via photo documentation (clinical data, macro-photos, histology) are essential tools. As it appears from our evaluation, cases of the convergent/complex type according to ICD10 present with the highest degree of difficulty in the external examination. This will very much depend on the timeliness of information of the existing pre-morbidities and their up-to-date status/therapy. As example, we refer to a female patient with a breast carcinoma 10 year prior, who dies of tumor cachexia; however, the oncologic disease was not known at the time of death to the clinician filling out the death certificate.

Emergently Available Medical Records May Save Lives

Finally, we are convinced that individual patient's medical records should be readily available in an emergency. For interaction in case of emergencies where a fast and protected exchange of medical history information is needed, a so-called telematic infrastructure is developed (in Europe). It allows data from the electronic patient file to be sent via App to end users (e.g. smart phones, tablets) or PCs. Since Jan 1, 2021, all health insurance companies in Germany have to supply their customers with such an App without extra costs. However, the use of this device is met with some skepticism regarding abuse; although patients have the control, which data they allow to be used by whom. Medical staff can only access this data, if the patient agrees. While electronic patient data files have been introduced in several countries in Northern Europe successfully (Estland 2001; Great Britain 2007; Sweden 2010), in others like Germany (2021) or Greece (2023) this has met much more resistance. Until this is an obligation for all patients, medical data collection by the patient's medical practitioner seems advantageous as an interim solution.

Conclusion

The present study analyzed the frequency of agreement/ of discrepancy between the cause of death listed in death certificates versus autopsy reports in a university hospital setting from 2005 – 2014. The patients (447) were 353 inpatients and 94 patients being sent from an outside hospital/as emergency (outpatients). While the number of deceased patients in the same time frame was about 15.000 only 1420 autopsies were done (about 9.4%) , of which only a limited number (447) could be used for this analysis because of missing clinical data/death certificates.

Overall, we found an agreement in 68%/ discrepancy in 32%, of which in 7% of cases no cause of death was given. Looking at nosological causal chains, an equal distribution was found for the linear/ divergent type in 21% versus 28.5% for the convergent/ complex type (Table 7). Furthermore, regarding the 143 cases with discrepant diagnoses, the frequency distribution between the different types was almost identical (Table 11). Thus, the frequency relation between the four nosological causal chains is maintained.

The valuation by classes using the Goldman criteria shows a combined major/type I error in 32%. This discrepancy is mainly due to the unknown diseases which accelerated a deteriorating health, and - because they were undiagnosed - had been left untreated.

While about 50% of outpatients were surgical cases, inpatients were cases from the internal medicine departments and only 12% came from general/vascular surgery. Myocardial infarct and cardiac insufficiency were the most frequent diseases followed by liver – and renal failure, gastrointestinal bleedings, and pulmonary insufficiency (Table 4).

Expectedly, the cause of death was mainly related to the 5 major categories (cardiac/circulatory failure; septicemia; myocardial infarct; respiratory failure and shock through internal bleeding (Table 8).

Looking at diseases most likely accompanying/accelerating causes of death main we could identifiy: arterial hypertension, pulmonary emphysema, arteriosclerosis, cardiac insufficiency, and coronary heart disease.

Oncologic diseases played only a relatively minor role except as forerunner of septicemia and respiratory failure. Unexpectedly, obesity and diabetes seem to play a rather small role (about 10% in all age groups): this may be due to the overall limited number of patients due to the high density of universities and major clinics in North Rhine Westfalia region. Overall, hypertension is the leading cause of death amounting from 15% at ages below 35 years to 35% in the patients over 70 years of age.

Author Statements

Ethics

Since human autopsy protocols and death certificates were analyzed, procedures were followed as outlined in accordance with ethical standards, formulated in the Helsinki Declaration 1975 (and revised in 1983), with pre- approval by the Ethic's Committee of the Medical Faculty of the University of Koeln (Koeln, Germany; file reference 20-1632).

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References

1. Kabra NS, Udani RH. Correlation between clinical diagnoses at the time of death and autopsy findings in clinically sick neonates at a regional neonatal intensive care unit in India. J Trop Pediatr. 2001; 47: 295-300.

2. Ong AW, Cohn SM, Cohn KA, Jaramillo DH, Parbhu R, McKenney MG, et al. Unexpected findings in trauma patients dying in the intensive care unit: results of 193 consecutive autopsies. J Am Coll Surg. 2002; 194: 401-6.

3. Fröhlich S, Ryan O, Murphy N, McCauley N, Crotty T, Ryan D. Discrepancies between clinical and autopsy diagnosis in liver transplant recipients—a case series. Acta Gastroenterol Belg. 2013; 76: 429-32.

4. Kuijpers CC, Fronczek J, van de Goot FR, Niessen HW, van Diest PJ, Jiwa M. The value of autopsies in the era of high-tech medicine: discrepant findings persist. J Clin Pathol. 2014; 67: 512-9.

5. Tai DY, El-Bilbeisi H, Tewari S, Mascha EJ, Wiedemann HP, Arroliga AC. A study of consecutive autopsies in a medical ICU: a comparison of clinical cause of death and autopsy diagnoses. Chest. 2001; 119: 530-6.

6. Twigg SJ, McCrirrick A, Sanderson PM. A comparison of postmortem findings with post hoc estimated clinical diagnoses of patients who die in a United Kingdom intensive care unit. Intensive Care Med^1. 2001; 27: 706-10.

7. Pastores SM, Dulu A, Voigt L, Raoof N, Alicea M, Halpern NA. Premortem clinical diagnoses and postmortem autopsy findings: discrepancies in critically ill cancer patients. Crit Care. 2007; 11: R48.

8. Friemann J. Klinische Obduktionen. Pathol Eur. 2010; 31: 256-67.

9. Goldman L, Sayson R, Robbins S, Cohn LH, Bettmann M, Weisberg M. The value of the autopsy in three medical eras. N Engl J Med. 1983; 308: 1000-5.

10. von Kress HF. Klinische Aspekte des Sterbens. [Clinical aspects of dying]. Naturwissenschaften. 1970; 57: 1-5.

11. Leiss J. Die Todesursache unter individual-pathologischen Gesichtspunkten. DMW. 1982; 107: 1069-72.

12. Wittekind C, Gradistanac T. Post-mortem examination as a quality improvement instrument. Dtsch Ärztebl Int. 2018; 115: 653-8.

13. Shojania KG, Burton EC, McDonald KM, Goldman L. Changes in rates of autopsy-detected diagnostic errors over time: a systematic review. JAMA. 2003; 289: 2849-56.

14. Wittekind C, Friemann J, Gradistanac T, Habeck J-O, Schalke W, Schulz-Schaeffer WJ. Leitline zur Durchführung von Obduktionen in der Pathologie. [Guidelines for autopsies in pathology] (in German). Publication from the Bundesverband Deutscher pathologen e. V. Deutsche Gesellschaft für Pathologie e.V. 2017.

15. Tavora F, Crowder CD, Sun CC, Burke AP. Discrepancies between clinical and autopsy diagnoses: a comparison of university, community, and private autopsy practices. Am J Clin Pathol. 2008; 129: 102-9.

16. Burton JL, Underwood J. Clinical, educational, and epide miological value of autopsy. Lancet. 2007; 369: 1471-80.

17. Winters B, Custer J, Galvagno SM Jr, Colantuoni E, Kapoor SG, Lee H, et al. Diagnostic errors in the intensive care unit: a sys tematic review of autopsy studies. BMJ Qual Saf. 2012; 21: 894-902.

18. Shojania KG, Burton EC. The persistent value of the autopsy. Am Fam Phys. 2004; 69: 2540-2.

19. Kuijpers CC, Fronczek J, van de Goot FR, Niessen HW, van Diest PJ, Jiwa M. The value of autopsies in the era of high-tech medicine: discrepant findings persist. J Clin Pathol. 2014; 67: 512-9.

20. Nemetz PN, Tanglos E, Sands LP, Fisher WP Jr, Newman WP 3rd, Burton EC. Attitudes toward the autopsy–an 8-state survey. MedGenMed. 2006; 8: 80.

21. Hull MJ, Nazarian RM, Wheeler AE, Black-Schaffer WS, Mark EJ. Resident physician opinions on autopsy importance and procurement. Hum Pathol. 2007; 38: 342-50.

22. Betz ME, Kelly SP, Fisher J. Death certificate inaccuracy and underreporting of injury in elderly people. J Am Geriatr Soc. 2008; 56: 2267-72.

23. Loeser H, Wittersheim M, Puetz K, Friemann J, Buettner R, Fries JW. Potential complications of transcatheter aortic valve implantation (TAVI)-an autopsy perspective. Cardiovasc Pathol. 2013; 22: 319-23.

24. Saleh MM, Büttner R, Fries JWU. Differentiation between pleura-mesothelioma versus pseudo-mesothelioma demonstrated in eight autopsy cases. Clin Oncol Res. 2021; 4: 2-7.

25. Tsitsikas DA, Brothwell M, Chin Aleong JA, Lister AT. The attitudes of relatives to autopsy: a misconception. J Clin Pathol. 2011; 64: 412-4.

26. Shojania KG, Burton EC. The vanishing nonforensic autopsy. N Engl J Med. 2008; 358: 873-5.

27. Midelfart J, Aase S. The value of autopsy from a clinical point of view. A survey of 250 general practitioners and hospital clinicians in the county of Sor-Trondelag, Norway. APMIS. 1998; 106: 693-8.

28. Feld K, Mellin W, Melzer B, Rothschild MA, Fries JWU. Fatal hemorrhage after tonsillectomy. A case of segmental mediolysis in arterioles. [Rechtsmedizin 2021 https://doi.org/10.1007/s00194-021-00502-8].