UCLA

UCLA Previously Published Works

Title

Treatable abdominal pathologic conditions and unsuspected malignant neoplasms at autopsy in veterans who received mechanical ventilation.

Permalink

<https://escholarship.org/uc/item/51r977ch>

Journal

JAMA, 265(7)

ISSN

0098-7484

Authors

Papadakis, MA
Mangione, CM
Lee, KK
et al.

Publication Date

1991-02-01

DOI

10.1001/jama.1991.03460070067044

Peer reviewed

Treatable Abdominal Pathologic Conditions and Unsuspected Malignant Neoplasms at Autopsy in Veterans Who Received Mechanical Ventilation

Maxine A. Papadakis, MD; Carol M. Mangione, MD; Kelvin K. Lee, PhD; Margaret Kristof, MS

Study Objective: To determine, in medical patients who received mechanical ventilation, the frequency and types of major unexpected diagnoses at autopsy that, if known before death, would probably have led to improved survival (class I errors) or substantively changed management but not survival (class IIB errors).

Design: Retrospective cohort study.

Setting: Six medical intensive care units in a Department of Veterans Affairs Cooperative Study.

Patients: One hundred seventy-two autopsied patients of the 401 veterans who received mechanical ventilation and died in the hospital.

Results: The class I error rate was 12%. Abdominal pathologic conditions—abscesses, bowel perforations, or infarction—were as frequent as pulmonary emboli as a cause of class I errors. While patients with abdominal pathologic conditions generally complained of abdominal pain, results of examination of the abdomen were considered unremarkable in most patients, and the symptom was not pursued. Six percent of patients had extensive malignant neoplasms (class IIB errors).

Conclusions: Atypical presentation of potentially treatable abdominal pathologic conditions is a common cause of class I errors in veterans who receive mechanical ventilation. Conversely, several patients with unrecognized terminal conditions underwent intensive intervention. If the information gained at autopsy had been known before death, management would have probably changed substantively in 18% of patients.

(JAMA. 1991;265:885-887)

CURRENTLY, the highest autopsy rate for nonforensic deaths is for patients who die in government-run hospitals.¹⁻⁸ Numerous studies have documented the importance of autopsies for patient care and medical education.⁴⁻⁸

Patients undergoing mechanical ven-

tilation receive the highest level of intensive care unit support. Our study aim was to examine the rates and types of unexpected major findings at autopsy in this group of patients in Department of Veterans Affairs medical centers (DVAMCs). As an adjunct to Department of Veterans Affairs (DVA) Cooperative Study Program (CSP) 333, "Prognosis of Mechanically Ventilated Medical Patients in Veterans Hospitals," the primary objective of which was to examine predictors of prognosis in veterans receiving mechanical ventilation in medical intensive care units, we examined autopsy findings in this cohort of patients.

PATIENTS AND METHODS

Setting

The six DVAMCs in DVA CSP 333 were in Durham, NC; Long Beach, Calif; Palo Alto, Calif; San Antonio, Tex; Seattle, Wash; and West Haven, Conn.

Patients

The sample included 651 consecutive medical patients who received mechanical ventilation some time during a 1- to 2-year period (January 1, 1986, to December 31, 1987). Postoperative patients and those whose primary reason for intensive care unit admission was cardiac were excluded. The mean inpatient mortality rate for the six sites was 62% (range, 43% to 71%), and 43% of those patients (range, 26% to 65%) had autopsies. The 401 veterans who died in the hospital and the 172 who had autopsies constitute the sample for this study.

Study Design and Data Collected

The research design was a retrospective cohort study. The patient's age, sex, clinical diagnoses, Acute Physiology and Chronic Health Evaluation II score,⁹ serum albumin level, and resuscitation status were abstracted.

Two board-certified internists (M.A.P. and C.M.M.) each reviewed approximately half of the medical records. Based on work by Goldman and colleagues,^{4,8} major unexpected autopsy findings were divided into two classes. Class I errors comprised major unexpected findings that would probably have led to a change in therapy and improved survival had they been diagnosed before death. A patient treated for bacterial pneumonia who, at autop-

From the Department of Medicine, University of California, San Francisco (Drs Papadakis and Mangione); the General Internal Medicine Section, Veterans Affairs Medical Center, San Francisco (Dr Papadakis and Ms Kristof); and the Department of Biostatistics, Veterans Affairs Medical Center, Palo Alto, Calif (Dr Lee). Dr Mangione is now with the Departments of Clinical Epidemiology and General Internal Medicine, Harvard Medical School, Boston, Mass.

Reprint requests to Department of Veterans Affairs Medical Center, 4150 Clement St 111A1, San Francisco, CA 94121 (Dr Papadakis).

Table 1.—Characteristics of 172 Autopsied Medical Veterans

	Mean ± SE*
Age, y	63.3 ± 0.8
Male gender, No. %	168 (98)
Days hospitalized	23.9 ± 2.3
Days of ventilation	6.7 ± 1.2
APACHE II score	28.9 ± 0.8
Predicted mortality (based on APACHE II score)	0.63 ± 0.02

*Unless otherwise indicated.

Table 2.—Clinicians' Primary Reasons for Admitting Autopsied Patients to the Medical Intensive Care Unit

	No. (%)
Pneumonia	15 (9)
Chronic obstructive pulmonary disease and pneumonia	9 (5)
Chronic obstructive pulmonary disease	11 (6)
Aspiration pneumonia	7 (4)
Post-respiratory arrest	7 (4)
Pulmonary embolus	4 (2)
Respiratory failure (other causes)	4 (2)
Sepsis	34 (20)
Gastrointestinal bleeding	19 (11)
Postcardiac arrest	16 (9)
Malignant neoplasm	10 (6)
Neurologic	8 (5)
Gastrointestinal	7 (4)
Intracerebral hemorrhage	4 (2)
Decompensated liver disease	3 (2)
Other	8 (5)
Unknown	6 (3)

sy, was found to have tuberculosis would be classified as having a class I error. Class II errors comprised major unexpected findings, the premortem diagnosis of which would probably not have changed management or survival.⁵ The investigators modified class II errors; class IIA represents the original Goldman class II. The new class is class IIB, which comprises major unexpected findings that, if known before death, would not have affected survival but would most likely have substantively changed management by restricting intensive care. Patients with unknown, widely metastatic adenocarcinoma would fit into this category. If this diagnosis had been known before death, it is probable that these patients would not have been admitted to the intensive care unit, or, if admitted to the intensive care unit, would not have received mechanical ventilation.

Whichever internist did not review the medical records performed a blind review of a random sample of 25% of charts without discordant autopsy findings and all class I and II findings. There was 100% concordance between the two internists.

Institutional review board approval was obtained from the University of California, San Francisco, and the San Francisco DVAMC Committee on Human Research.

Table 3.—Class I, Class IIA, and Class IIB Diagnosis Errors in Major Unexpected Autopsy Findings in 172 Patients*

Diagnosis	No. (%) of Patients†		
	Class I	Class IIA	Class IIB
Abdominal pathologic condition	9 (5)	4 (2)	...
Abdominal abscess	2 (1)	...	...
Bowel perforation	4 (2)	1 (1)	...
Bowel infarction	2 (1)	...	...
Retroperitoneal hemorrhage	...	2 (1)	...
Ruptured abdominal aortic aneurysm	1 (1)	...	...
Colitis	...	1 (1)	...
Cardiovascular disease	7 (4)	7 (4)	...
Pulmonary embolism	7 (4)	2 (1)	...
Myocardial infarction	...	4 (2)	...
Endocarditis	...	1 (1)	...
Infection	5 (3)	5 (3)	...
Fungal	2 (1)	5 (3)	...
Tuberculosis	3 (2)	...	...
Cancer	...	...	11 (6)
Lung	...	...	4 (2)
Gastrointestinal	...	...	5 (3)
Leukemia	...	...	1 (1)
Prostate	...	...	1 (1)

*Diagnosis of class I errors probably would have led to a change in treatment; diagnosis of class IIA errors probably would not have led to a change in treatment; and diagnosis of class IIB errors probably would have changed treatment by limiting intensive care.

†Each patient is represented once, and the most clinically significant diagnosis is listed.

Statistical Analysis

Proportions were compared with a χ^2 test.¹⁰ Continuous variables were compared by analysis-of-variance procedures. Statistical significance was set at .05.¹⁰

RESULTS

Characteristics of the autopsied patients are shown in Table 1. Most were older men, reflecting the population served by DVAMCs. The mean APACHE II score was 28.9, with 63% predicted mortality.⁹ There were no statistically significant differences in demographic or clinical characteristics in Table 1 between the 172 autopsied and 229 nonautopsied patients ($P > .65$) or among the study sites. The clinicians' most common primary diagnoses necessitating admission to the medical intensive care unit for the autopsied patients are shown in Table 2.

Unexpected Autopsy Findings

The Class I and II error rates were 12.2% and 15.5%, respectively (Table 3). Forty-two percent of the class II errors were class IIB errors. Five of the 48 patients had 12 class I or II errors, and the remaining patients had single errors. Interhospital comparisons were not feasible because of small sample size. When patients with class I errors were compared with the remainder of the autopsied cohort, none of the following variables predicted class I errors in

a univariate analysis: patient age, days hospitalized, days receiving ventilation, APACHE II score, serum albumin concentration at hospital admission, serum albumin concentration at initiation of mechanical ventilator assistance, and presence of a do-not-resuscitate order at least 24 hours before death. There were no variables predictive of class IIB errors, but the sample size was small.

Clinical characteristics of the patients with treatable abdominal pathologic conditions at the time mechanical ventilation was initiated are seen in Table 4. While the majority complained of abdominal pain and had heme-positive stools, results of examination of the abdomen were considered otherwise benign, with no elicitable tenderness and present bowel sounds. Only 25% of patients were febrile, and 60% had abnormal white blood cell counts. In two thirds of patients, the clinicians did not consider and pursue the class I diagnosis with diagnostic procedures. Comorbid conditions included alcoholism, alcoholic liver disease, and cerebrovascular accident.

The mean (SE) age of the 11 patients with class IIB errors was 68.5 ± 2.7 years, and the APACHE II score was 26.9 ± 2.5 . They were hospitalized 25.4 ± 8.2 days, and they spent 12.9 ± 4.3 days in the intensive care unit and 10.2 ± 4.2 days receiving ventilator assistance. The carcinomas were metastatic in all cases but one. The clinicians' diagnosis in the four patients with pri-

Table 4.—Characteristics of the 8 Patients With Class I Abdominal Abscesses, Perforation, or Infarction at the Time of Initiation of Mechanical Ventilation

	Patient							
	1	2	3	4	5	6	7	8
Temperature, °C	36.9	35.9	36.5	36.4	38.2	36.8	37.0	39.1
Mean arterial pressure, mm Hg	0	83	127	94	77	60	79	56
White blood cell count, $\times 10^3$ (polymorphonuclear leukocytes, %)	8.7	15.0	24.5 (96.5)	8.8 (60.1)	13.2 (21)	7.8 (78)	23.8	22
Bowel sounds	Yes	Yes	Yes	Yes	Yes	Yes	NA	Faint
Subjective abdominal pain	Diffuse	Yes	Yes	NA	NA	Yes	Yes	No
Abdominal tenderness on examination	No	No	Yes	No	No	Mild	Yes	Equivocal
Blood cultures	Negative	NA	<i>Enterobacter</i> species	Negative	Negative on antibiotics	<i>Escherichia coli</i>	<i>E coli</i>	<i>Klebsiella</i> species
Heme-positive stools	Yes	No	Yes	Yes	NA	Yes	NA	Yes
Clinician's diagnosis	Morbid obesity, corticosteroids, urosepsis	Pulmonary embolus	Abdominal vasculitis	Alcoholic liver disease	Sepsis	Spontaneous bacterial peritonitis	Alcoholism, Hypotension	Urosepsis
Class I diagnosis	Sigmoid perforation	Duodenal ulcer perforation	Atherosclerotic colonic infarction	Abdominal wall abscess to jejunum	Subdiaphragmatic abscess	Duodenal ulcer perforation	Bowel infarction	Bowel perforation

mary or metastatic carcinoma in the lungs was pneumonia.

COMMENT

The high autopsy rate in this DVA Cooperative Study affords us the opportunity to study class I and II error rates in the unique cohort of veterans receiving mechanical ventilation. Our class I error rate of 12% is consistent with those in university and community hospitals, as described by Goldman et al⁴ and Landefeld et al.⁵

The class I errors in veterans receiving mechanical ventilation were diagnoses of pulmonary emboli, abdominal pathologic conditions, or infection. Pulmonary embolus is recognized as a leading cause of class I errors.^{4,5} In our cohort, pulmonary embolus was also a frequently missed diagnosis, accounting for one third of the class I errors. An important new finding was that 39% of class I errors were potentially treatable abdominal pathologic conditions—abscesses, bowel perforations, or infarction. In addition, many of the usual clinical signs and symptoms of acute surgical abdomens were absent in this critically ill population. While patients generally complained of some abdominal pain, body temperature, results of examination of the abdomen, and results of the usual laboratory tests were considered unremarkable in many. The diagnoses were missed in two thirds of patients because the clinicians failed to consider and pursue the diagnoses, not because clinicians were misled by inconclusive or incorrect information from diagnostic procedures, such as computed tomographic scans or abdominal ultrasound. Possible reasons for the absence of typi-

cal presentations of acute abdominal conditions in half the patients include corticosteroid use, alcoholism, alcoholic liver disease, and cerebrovascular accident.

The high frequency of application of intensive care treatment to patients with unrecognized terminal conditions is also an important lesson of this autopsy study. The findings have implications for a decision to use intensive intervention and also for the allocation of limited intensive care unit resources.

The limitations of this study are those of a retrospective study design, namely, that the available data on which we based our conclusions came only from chart documentation. Despite our high autopsy rate and lack of demonstrable difference in demographic and clinical characteristics between autopsied and nonautopsied patients, autopsied patients may represent selection bias, and caution must be exercised in extrapolating to the group at large.

Atypical presentation of potentially treatable abdominal pathologic conditions was the most frequent class I error in patients receiving mechanical ventilation in these six DVAMCs. Since the results of abdominal examination and laboratory data were frequently remarkably benign, the clinician must be vigilant, especially if the patient complains of abdominal pain. At this point, we cannot say whether the class IIB error rate is unique to this cohort.

If the information gleaned from this autopsy study were known before death, patient management would have changed substantively in 18% of cases. The frequency of atypical presentations of treatable conditions and the failure to

detect a terminal condition when it is present emphasize the importance of continuing to obtain autopsies in this era of diagnostic technological advances.

This study was supported by the Department of Veterans Affairs Cooperative Studies Program of the Veterans Health Services and Research Administration.

We gratefully acknowledge the invaluable assistance of Sylvia Miles, Michael R. Jeung, and Lenore Sheridan during this study.

Veterans Affairs Medical Centers from the following cities participated in Department of Veterans Affairs Cooperative Study Project 333 (names of coordinators are given): Durham, NC: David Matchar, MD; Long Beach, Calif: Robin Onishi, MD; Palo Alto, Calif: James Hallenbeck, MD; San Antonio, Tex: Raymond Ramusack, MD; Seattle, Wash: Daniel Kent, MD; and West Haven, Conn: David Lee, MD.

References

1. Roberts WC. The autopsy: its decline and a suggestion for its revival. *N Engl J Med.* 1978; 299:332-338.
2. Centers for Disease Control. Autopsy frequency—United States, 1980-1985. *MMWR.* 1988;37:191-194.
3. Reichart CM, Kelly VL. Prognosis for the autopsy. *Health Aff.* 1985;4:82-92.
4. Goldman L, Sayson R, Robbins S, Cohn LH, Bettman M, Weisberg M. The value of the autopsy in three medical eras. *N Engl J Med.* 1983;308: 1000-1005.
5. Landefeld CS, Chren M, Myers A, Geller R, Robbins S, Goldman L. Diagnostic yield of the autopsy in a university hospital and a community hospital. *N Engl J Med.* 1988;318:1249-1254.
6. McPhee S, Bottles K. Autopsy: moribund art or vital science? *Am J Med.* 1985;78:107-113.
7. Lundberg GD. Now is the time to emphasize the autopsy in quality assurance. *JAMA.* 1988;260: 3488.
8. Kircher T, Nelson J, Burdo H. The autopsy as a measure of accuracy of the death certificate. *N Engl J Med.* 1985;313:1263-1269.
9. Knaus WA, Draper EA, Wagner DP, Zimmerman JE. APACHE II: a severity of disease classification system. *Crit Care Med.* 1985;13:818-829.
10. Fleiss JL. *Statistical Methods for Rates and Proportions.* 2nd ed. New York, NY: John Wiley & Sons Inc; 1981.