ORIGINAL INVESTIGATION

Clinical and Autopsy Diagnoses in the Intensive Care Unit

A Prospective Study

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Background: Autopsy rates have declined worldwide, but recent retrospective intensive care unit (ICU) data indicate major discrepancies between more than 25% of clinical and autopsy diagnoses.

Methods: We conducted a 3-year prospective study of all consecutive autopsies performed on patients who died in a university hospital medical-surgical ICU to determine how many might have benefited from a different level of care, had the autopsy diagnosis been made before death. All clinical diagnoses were compared with autopsy findings at monthly clinical-pathological meetings. Major and minor diagnostic discrepancies were categorized according to the criteria of Goldman et al.

Results: Of 1492 patients admitted to the ICU, 315 died, of whom 167 (53.0%) were autopsied. The most common reason (79.7%) for not obtaining an autopsy was family refusal. The mean ± SD clinical characteristics were similar for autopsied vs nonautopsied patients, except for shorter length of ICU stay (13 ± 17 vs 20 ± 27 days, $P = .006$), shorter duration of mechanical ventilation (13 ± 16 vs 19 ± 25 days, $P = .01$), and lower percentage of postcardiac surgery patients (38.9% vs 50.0%, $P = .05$). Among the intensivists' 694 clinical diagnoses, 33 (4.8%) were refuted and 13 (1.9%) were judged incomplete by autopsy findings. Autopsies revealed 171 missed diagnoses, including 21 cancers, 12 strokes, 11 myocardial infarctions, 10 pulmonary emboli, and 9 endocarditis, among others. Major diagnostic errors (class I and class II discrepancies) were made in 53 (31.7%) of 167 patients, with a high percentage of immunocompromised patients also observed among these. Similar percentages of patients with class I and class II errors vs other patients had undergone modern diagnostic techniques during their ICU stay.

Conclusion: Even in the era of modern diagnostic technology, regular comparisons of clinical and autopsy diagnoses provide pertinent information that might improve future management of ICU patients.

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During the past few decades, autopsy rates have fallen worldwide: in the United States, they decreased from 41% in the 1960s to 22% in the 1970s,[1] and, in France, from 15.4% in 1988 to 3.7% in 1997.[2] The reasons for this decrease are many: the time-consuming task of autopsies for pathology departments, fear of potential legal repercussions (should misdiagnoses be discovered), reluctance of families to give permission for the procedure, and doubt concerning the value of the examination in the era of modern diagnostic techniques.[3-5] The authors of several recent retrospective intensive care unit (ICU) studies[3,6-10] reported rates of major discrepancies between clinical and autopsy diagnoses ranging between 19% and 27%. However, to date, no prospective study has examined the diagnostic contribution of autopsy in the ICU setting.

To fill this void, we prospectively analyzed all consecutive autopsies during 3 years performed on patients who died in our tertiary care medical-surgical ICU. Our objectives were to assess the accuracy of clinical diagnoses among a large cohort of ICU patients and to determine how many patients might have benefited from modified care, had the autopsy diagnosis been made before death.

METHODS

PATIENTS

This prospective study was conducted from November 1, 1995, to November 1, 1998, in a 17-bed ICU in a large, 1200-bed, university hospital. The protocol was in accord with the ethical standards of the Committee for the Protection of Human Subjects at our hospital, which waived the need for informed consent.

Critically ill patients admitted to our tertiary ICU (60% medical and 40% surgical,

mostly postcardiac) include those originating from the medical wards of the hospital, cardiac surgery patients with postoperative multiple organ failure and/or infections or nonsurgical patients admitted via the emergency department, and medical and surgical patients referred to us from other ICUs. On ICU admission, each patient's hospital chart was constructed prospectively, and the following data were recorded: age; sex; severity of the underlying medical condition, stratified according to the criteria of McCabe and Jackson[11]; presence or absence of immunosuppression (oral intake of >20 mg of methylprednisolone or its equivalent for >6 months; chemotherapy during the preceding 6 months; oral intake of any dosage of cyclosporine, methotrexate, or azathioprine; or a diagnosis of cancer, leukemia, or acquired immunodeficiency syndrome); and Simplified Acute Physiology Score II.[12]

For patients who died in the ICU, the following data were collected: length of ICU stay, duration of mechanical ventilation, and number of radiological (ultrasonography and computed tomographic scan) and fiberoptic bronchoscopy diagnostic procedures performed during the ICU stay.

Furthermore, all clinical diagnoses were determined (based on consensus) and the suspected cause of death was noted within 24 hours of death (before the autopsy) at the daily meetings of all the ICU intensivists and were reported on a specific form, using the codes of the *International Classification of Diseases, Ninth Revision*.[13]

POSTMORTEM EXAMINATION

Our routine is to perform an autopsy, when legally possible, on all patients who die in our ICU (not just those in whom the cause of death is uncertain). According to a 1994 French bioethics law, the treating physician of a patient who died can request an autopsy if the patient had not expressed opposition before dying. However, authorization must also be obtained from family members. If no opposition was expressed, the autopsy, including histological examination of all organs and the brain, when indicated, was performed by a hospital pathologist. A senior member of the ICU team treating the patient also attended the autopsy.

CORRELATION OF CLINICAL AND AUTOPSY DIAGNOSES

Monthly clinical-pathological meetings were held to compare clinical and autopsy diagnoses. Results of these correlations were classified as follows: clinical diagnosis confirmed by the autopsy, incomplete clinical diagnosis, clinical diagnosis refuted by the autopsy, clinical diagnosis impossible to confirm because of an incomplete autopsy, clinical diagnosis impossible to confirm by the autopsy, and autopsy diagnosis missed by the clinicians. Furthermore, discrepancies between clinical and autopsy diagnoses were classified according to the criteria of Goldman et al[14] as follows: class I, missed major diagnosis that, had it been made, would have changed patient management and might have resulted in cure or prolonged survival; class II, missed major diagnosis that would not have modified ongoing patient care; class III, missed minor diagnosis associated with the terminal disease but not directly responsible for death; and class IV, other missed minor diagnoses. Discrepancies were classified based on consensus by the intensivists and the pathologists during the meeting. In the case of discordance between them, the pathologists' diagnosis was retained.

STATISTICAL ANALYSIS

Continuous variables were compared with the *t* test, and percentages were compared with the χ^2 tests. Statistical significance was set at $P<.05$.

RESULTS

STUDY POPULATION

During the study, 1492 patients were admitted to our ICU, of whom 315 (21.1%) died during their ICU stay and 167 (53.0%) were autopsied. The other 148 patients were not autopsied for the following reasons: family refusal (118 patients [79.7%]), inability to contact family members (21 patients [14.2%]), and family desire for a rapid funeral for personal or religious reasons (9 patients [6.1%]). A comparison of the clinical characteristics between autopsied and nonautopsied patients is shown in **Table 1**: only the length of ICU stay and duration of mechanical ventilation were significantly shorter for autopsied patients. The lower percentage of postcardiac surgery patients who were autopsied trended toward significance. No other characteristic differed significantly between the 2 groups.

COMPARISON OF CLINICAL AND AUTOPSY DIAGNOSES

For the 167 autopsied patients, 1308 clinical diagnoses before death (mean±SD, 7±6 diagnoses per patient) were recorded. Among them, 614 were impossible to verify by the postmortem examination (eg, functional renal failure, cardiac arrhythmia, or septicemia). Of the 694 remaining diagnoses, 621 (89.5%) were confirmed, 33 (4.8%) were refuted (**Table 2**), 27 (3.9%) were not assessed because of an incomplete autopsy examination, and 13 (1.9%) were considered incomplete by autopsy findings. Clinicians most frequently erroneously diagnosed cancer, endocarditis, myocardial infarction, and pneumonia (Table 2). One hundred seventy-one diagnoses were missed by the intensivists and discovered at autopsy. The most frequently missed diagnoses were infarction and thrombosis: 26 infarctions (11 myocardial, 11 spleen, 2 renal, and 2 mesenteric), 12 strokes (7 ischemic and 5 hemorrhagic), and 10 pulmonary emboli. Other frequently missed diagnoses were cancer (6 lung, 5 kidney, 3 prostate, 2 lymphoma, and 5 other) and infections (9 endocarditis and 8 abscesses).

Classification of the 219 discordant clinical and autopsy diagnoses according to the criteria of Goldman et al identified 20 class I errors in 17 (10.2%) of 167 patients, 55 class II errors in 44 patients (26.3%), 69 class III errors in 46 patients (27.5%), and 75 class IV errors in 54 patients (32.3%). There were no discrepancies between the clinical and autopsy diagnoses in 52 (31.1%) of 167 patients. Major diagnostic errors (class I and class II) were noted in 53 patients (31.7%). **Table 3** summarizes the class I discrepancies between clinical and autopsy diagnoses. Seven (41.2%) of the 17 patients with class I errors were immunocompromised at ICU admission.

A comparison of the clinical characteristics between patients with major (class I and class II) diagnostic discrepancies and other autopsied patients is shown in Table 1. We noted a higher percentage of immunocompromised patients in the class I and class II groups. These patients also had lower disease severity scores at ICU admission. No other significant differences were noted between the 2 groups. However, the percentages of patients undergoing computed tomographic scan, ul-

Table 1. Clinical Characteristics of the Patients Who Died in the Intensive Care Unit (ICU) and of Autopsied Patients With or Without Major Diagnostic Discrepancies*

Characteristic	Patients Who Died in the ICU			Autopsied Patients		
	No Autopsy (n = 148)	Autopsy (n = 167)	*P* Value	Class I or II† (n = 53)	Others (n = 114)	*P* Value
ICU admission characteristics						
Age, y, mean (SD)	67 (14)	65 (14)	.24	64 (14)	65 (14)	.71
Male sex	95 (64.2)	96 (57.4)	.25	31 (58.4)	65 (57.0)	.87
McCabe and Jackson[11] score ≥2	100 (67.6)	112 (67.1)	.92	41 (77.4)	71 (62.3)	.08
Immunocompromised status	32 (21.6)	33 (19.8)	.78	20 (37.7)	13 (11.4)	<.001
Postcardiac surgery patient	74 (50.0)	65 (38.9)	.05	24 (45.3)	41 (36.0)	.30
Glasgow Coma Scale score, mean (SD)	10.4 (5.2)	10.5 (4.9)	.84	11.4 (4.9)	10.0 (4.9)	.10
Simplified Acute Physiology Score II, mean (SD)	63 (23)	62 (22)	.76	58 (22)	64 (22)	.10
ICU events						
ICU length of stay, d, mean (SD)	20 (27)	13 (17)	.006	12 (12)	14 (18)	.55
Duration of mechanical ventilation, d, mean (SD)	19 (25)	13 (16)	.01	12 (12)	14 (18)	.50
Computed tomographic scan	52 (35.1)	53 (31.7)	.52	15 (28.3)	38 (33.3)	.60
Ultrasonography	111 (75.0)	127 (76.0)	.82	44 (83.0)	83 (72.8)	.18
Fiberoptic bronchoscopy	87 (58.8)	94 (56.3)	.65	27 (50.9)	67 (58.8)	.40

*Data are given as number (percentage) unless otherwise indicated.
†Major diagnostic discrepancies according to the criteria of Goldman et al.[14]

trasonography, or fiberoptic bronchoscopy were high, and most of the patients with class I and class II errors associated with the cardiovascular system underwent echocardiography during their ICU stay. Specifically, the patients with class I missed diagnoses of endocarditis, pericarditis, and aortic dissection underwent transthoracic echocardiography in the week preceding their death.

COMMENT

The aim of this study was to prospectively evaluate the accuracy of clinical diagnoses and to determine how many ICU patients might have received modified care if the autopsy diagnosis had been made before death. With an autopsy rate of 53.0%, major diagnostic errors were identified for 31.7% of the autopsied patients, and the correct diagnosis would have changed management and possibly resulted in a cure or prolonged survival for up to 10% of the patients.

To the best of our knowledge, this study is the first to date to prospectively evaluate the potential contribution of autopsies to the management of future ICU patients. Our 53.0% autopsy rate falls in the upper range of those reported in retrospective ICU studies[6,9,15] (22%-51%), except for the 93% rate obtained by Roosen et al,[3] from Belgium, a country with an autopsy-favorable legal system. Factors explaining lower autopsy rates mostly reflect the cost and the lack of time available for this labor-intensive procedure, fear of litigation, reluctance of family members to give permission for the examination, and the increased confidence in the performance of modern diagnostic techniques.

Previous retrospective studies[3,6,8,9] comparing clinical and autopsy diagnoses for ICU patients reported major (class I and class II) discrepancy rates ranging from 19.8% to 27%. Our rate was even higher (31.7%). These differences in major discrepancy rates among studies may be explained by different ICU populations (medical vs surgical),[8] higher percentages of immunocompromised patients,[8] different autopsy policies (higher discrepancy rates when autopsies are performed only in the case of uncertain diagnosis), and study design (retrospective vs prospective).

Table 2. Clinical vs Autopsy Diagnoses*

Diagnosis	Autopsy-Identified Missed Clinical Diagnosis	Autopsy-Refuted Clinical Diagnosis
Cancer	21 (12.3)	3 (9.1)
Myocardial infarction	11 (6.4)	3 (9.1)
Stroke	12 (7.0)	1 (3.0)
Spleen infarction	11 (6.4)	0
Renal infarction	2 (1.2)	0
Mesenteric infarction	2 (1.2)	1 (3.0)
Pulmonary embolism	10 (5.9)	0
Endocarditis	9 (5.3)	3 (9.1)
Abscesses, cellulitis	8 (4.7)	0
Pericarditis	6 (3.5)	0
Pancreatitis	4 (2.3)	1 (3.0)
Pneumonia	0	3 (9.1)
Herpes infection	0	2 (6.1)
Meningitis	0	1 (3.0)
Valvular heart disease	0	2 (6.1)
Aortic dissection	0	2 (6.1)
Hemorrhage	9 (5.3)	0
Disseminated intravascular coagulation	0	2 (6.1)
Cirrhosis	0	2 (6.1)
Intrapericardial foreign body	1 (0.6)	0
Other diagnoses	65 (38.0)	7 (21.2)
Total	**171**	**33**

*Data are given as number (percentage).

As pointed out by Goldman and colleagues,[14,16] major discrepancy rates remained stable over time (around 10% in the 1960s, 1970s, and 1980s), and the percentage of missed diagnoses did not decrease between 1912 and the end of the 20th century. This observation can be explained by the different types of patients being treated during the 20th century. Advances in medical therapies, such

Table 3. Class I Discrepancies Between Clinical and Autopsy Diagnoses That Would Have Changed Therapy

Clinical Diagnosis	Autopsy Diagnosis	Different Management*
Digestive tract hemorrhage	Aortic dissection	Surgery
Shock of unknown origin	Ruptured aortic aneurysm	Surgery
Shock of unknown origin	Hemopericardium	Surgery
Acute respiratory failure	Postoperative para-aortic valve leakage	Surgery
Septic shock	Intrapericardial foreign body (gauze)	Surgery
Shock of unknown origin	Perforated gastric ulcer	Surgery
Shock of unknown origin	Perforated duodenal ulcer	Surgery
Shock of unknown origin	Small-bowel obstruction (adhesions)	Surgery
Digestive tract hemorrhage	Ruptured gastric suture	Surgery
Postanoxia encephalopathy	Subdural hematoma	Surgery
Idiopathic myocardiopathy	Endocarditis	Antibiotics
ARDS	Mitral endocarditis	Antibiotics
Septic shock	Diffuse aspergillosis	Antifungal therapy
Gram-negative septic shock	Diffuse CMV disease	Anti-CMV therapy
ARDS	CMV pneumonia	Anti-CMV therapy
Shock of unknown origin	Stroke	Antiaggregating agents
Septic shock	High-grade lymphoma	Chemotherapy
ARDS	High-grade lymphoma	Chemotherapy
Bacterial meningitis	High-grade lymphoma	Chemotherapy
Pulmonary fibrosis	Carcinomatous lymphangitis	Chemotherapy

Abbreviations: ARDS, acute respiratory distress syndrome; CMV, cytomegalovirus.
*Had the autopsy diagnosis been made before death.

as organ transplantation and chemotherapy, have prolonged life expectancy, but new diseases and new complications have emerged, especially opportunistic infections. In addition, although the advancement of modern diagnostic techniques has improved the accuracy of certain clinical diagnoses, some diseases remain particularly challenging to identify. For example, the available methods to diagnose fungal infections do not reliably differentiate between colonization and systemic infections, distal pulmonary emboli can be missed on computed tomographic scan, and endocarditis can be overlooked on transesophageal echocardiography. In this study, the percentages of patients undergoing at least 1 sophisticated diagnostic examination did not differ between class I/II patients and other patients. Furthermore, new diagnostic procedures, such as ultrasonography and computed tomographic scans, can yield false-positive and false-negative diagnoses for 6% to 9% of patients.[17] Indeed, 3 cases of suspected endocarditis and 2 cases of aortic dissection were subsequently refuted by the autopsy diagnoses in the present study.

Our study has several limitations. First, the autopsy rate was only 53.0%. However, this study is the first to date in the ICU setting with a strict prospective design, and our sample size strengthened the validity of our results. The reason for not performing autopsies was almost exclusively family refusal, and our autopsy rate compares favorably with rates reported in retrospective ICU series. Second, our results may not be applicable to other ICU populations. Many patients are referred to our ICU after prolonged stays in another department, hospital, or ICU, and more than 40% of the patients included in this study were treated for severe complications of cardiac surgery. These factors may account for our high rate of major diagnostic discrepancies.

In conclusion, the rate of discrepant autopsy findings remains high, despite major technical advances in diagnostic methods during the past 50 years. Diagnosing ICU patients is particularly challenging because of the inability of these patients to give their medical histories, the severity of their diseases (which has increased during the past decades), and the high incidence of nosocomial and opportunistic infections in these patients. At the beginning of the 21st century, autopsies still have a major role to play in assuring and improving the quality of medical care by monitoring diagnostic accuracy and treatment of the ICU patient. Finally, as pointed out by Durning and Cation[10] in a recent survey of internal medicine residents, autopsies are a valuable educational tool, and autopsy attendance should remain an integral part of residency training.

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REFERENCES

1. Roberts WC. The autopsy. *N Engl J Med.* 1978;299:332-338.
2. Chariot P, Witt K, Pautot V, et al. Declining autopsy rate in a French hospital. *Arch Pathol Lab Med.* 2000;124:739-745.
3. Roosen J, Frans E, Wilmer A, Knockaert DC, Bobbaers H. Comparison of premortem clinical diagnoses in critically ill patients and subsequent autopsy findings. *Mayo Clin Proc.* 2000;75:562-567.
4. Kleiner DE, Emmert-Buck MR, Liotta LA. Necropsy as a research method in the age of molecular pathology. *Lancet.* 1995;346:945-948.
5. Rosenbaum GE, Burns J, Johnson J, et al. Autopsy consent practice at US teaching hospitals: results of a national survey. *Arch Intern Med.* 2000;160:374-380.
6. Tai DY, El-Bilbeisi H, Tewari S, et al. A study of consecutive autopsies in a medical ICU. *Chest.* 2001;119:530-536.
7. 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.* 2001;27:706-710.
8. Mort TC, Yeston NS. The relationship of premortem diagnoses and postmortem findings in a surgical intensive care unit. *Crit Care Med.* 1999;27:299-303.
9. Blosser SA, Zimmerman HE, Stauffer JL. Do autopsies of critically ill patients reveal important findings that were clinically undetected? *Crit Care Med.* 1998; 26:1332-1336.
10. Durning S, Cation L. The educational value of autopsy in a residency training program. *Arch Intern Med.* 2000;160:997-999.
11. McCabe WR, Jackson GG. Gram-negative bacteremia, I: etiology and ecology. *Arch Intern Med.* 1962;110:847-855.
12. Le Gall JR, Lemeshow S, Saulnier F. A new Simplified Acute Physiology Score (SAPS II) based on a European/North American multicenter study. *JAMA.* 1993; 270:2957-2963.
13. World Health Organization. *International Classification of Diseases, Ninth Revision (ICD-9).* Geneva, Switzerland: World Health Organization; 1978.
14. 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;308:1000-1005.
15. Gut AL, Ferreira AL, Montenegro MR. Autopsy. *Intensive Care Med.* 1999;25: 360-363.
16. Goldman L. Diagnostic advances vs the value of the autopsy: 1912-1980. *Arch Pathol Lab Med.* 1984;108:501-505.
17. Kirch W, Schafii C. Misdiagnosis at a university hospital in 4 medical eras. *Medicine* (Baltimore). 1996;75:29-40.