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Clinical-pathological discrepancies in critically ill patients with difficult premortem diagnoses

Discrepâncias clínico-patológicas em pacientes graves com difícil diagnóstico pre-mortem

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ABSTRACT

Introduction: The importance of autopsies is a common theme of discussion both in Brazil and around the world, as it elucidates causes of death and has wide-ranging social value. However, the practice of autopsies is gradually coming to be considered unnecessary, and over the last several years, there has been a decline in the number of postmortem examinations.

Objectives: To compare clinical and pathological diagnoses in critically ill patients with difficult premortem diagnoses.

Methods: All autopsy cases (98 cases) from any of the three general medical/surgical intensive care units (78 beds in total) affiliated with the medical school

from January 2003 to December 2006 were analyzed. We evaluated the clinical and pathological diagnoses based on the Goldman criteria.

Results: Forty-nine (50%) cases were classified as Goldman classes I and II. In contrast, only 30 (30.6%) cases had complete agreements between premortem and postmortem diagnoses and were classified as class V. Infections had a significantly greater rate of concordant diagnosis than did cardiovascular diseases.

Conclusion: We identified significant discrepancies between clinical and pathological findings, reinforcing the value of postmortem examination.

Keywords: Autopsy; Clinical diagnosis; Critical care

This study was conducted at the Faculdade de Medicina de São José do Rio Preto - FAMERP – São José do Rio Preto (SP), Brazil.

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INTRODUCTION

The importance of autopsies is a common theme of discussion both in Brazil and around the world, as it elucidates causes of death and has wide-ranging social value. Autopsies provide both unique insights into diagnoses and feedback to the physicians involved in patient care regarding the accuracy of their evaluations and the effectiveness of their treatments. Certainly, autopsies contribute to medical education and benefit future patients. Due to the paucity of data, autopsy studies of critically ill patients in particular are needed in Brazil. However, this is a practice that is gradually being perceived as unnecessary.

Many studies have shown a decline in adult postmortem examination rates worldwide. In Australia, rates have dropped from 21% at the start of the 1990s to approximately 12% in 2003.⁽¹⁾ In the United States of America, the rate of autopsy was as low as 5% in 2002.⁽²⁾ The decline in the number of postmortem exams does not necessarily mean that the accuracy of clinical diagnoses has improved or that advanced diagnostic methods have substituted this practice.⁽³⁻⁵⁾

Great discrepancies have been observed between clinical diagnoses and autopsy results.^(5,6) This divergence can vary depending on the institution that performed the autopsy; Jayawardena et al. reported a very high agreement in 75% of cases, and Pastores et al. obtained a rate of 74% agreement.^(7,8)

However, Valdez-Martínez et al. recorded agreement in only 43% of cases.⁽⁹⁾ Studies in the USA have shown that if the postmortem findings had been discovered earlier, there would have been changes in the therapeutic approach in approximately 16% of cases, with a consequent increase in survival.⁽¹⁰⁾ In 1983, these discrepancies were classified by Goldman et al. in terms of their importance in clinical practice, suggesting that attention should be given to therapeutically significant errors whose corrections could contribute to improvements in medical care.⁽¹¹⁾

Previous studies in patients admitted to intensive care units (ICUs) have shown that premortem clinical diagnoses are frequently incorrect compared to postmortem examinations, and in up to 39% of patients, a treatable condition is identified upon postmortem examination that might have altered the outcome of the patient if the condition had been recognized premortem.^(12,13) Thus, this study aims to review postmortem examinations of patients admitted over four consecutive years to ICUs in a tertiary hospital and to compare clinical and autopsy diagnoses.

METHODS

This retrospective cross-sectional study was performed in a 718-bed public teaching hospital that provides primary to tertiary care. A total of 409 deaths that occurred during the study period, which included deaths involving all diseases and all medical specialties, were identified.⁽¹⁴⁾ Patients who stayed for less than one hour in the hospital and those involving children under 15 years of age were excluded. The study protocol was approved by the local Ethics Committee, which waived the need for informed consent.

All autopsy cases from any of the three general medical/surgical ICUs (78 beds in total) affiliated with a medical school from January 2003 to December 2006 were analyzed. Autopsies were performed by six pathologists after medical request and family consent. Autopsies were requested only when there was doubt about the clinical diagnosis.

Out of 119,091 hospital admissions between 2003 and 2006, deaths occurred in 8127 (6.8%) cases, and of these cases, autopsies were performed in 650 (8%) cases. ICUs autopsy requests totaled 98 (15.07%) cases and were included in this research. One internist, a senior pathologist and two general clinicians analyzed the medical records and the autopsy reports. Data were recorded for each patient, including age, gender, length of stay in the hospital, referring facility, medical history, medical evolution, clinical diagnosis and macroscopic and microscopic autopsy diagnoses. To obtain clinical diagnoses, we analyzed not only the diagnoses on the medical and autopsy records but also if the recommended treatment was administered to the patient, even though the patient diagnoses was not registered in the medical record. Then, we coded the diagnoses based on the International Statistical Classification of diseases (ICD-10).

The comparison between clinical and autopsy findings followed the Goldman criteria (Table 1). For the purpose of analysis, diagnoses classes I and II were grouped as discordance, and classes III and IV, along with class V, were grouped as concordance.

Table 1 - Goldman criteria for autopsy discrepancies

Class I	Missed major diagnosis with a potential adverse impact on survival that would have changed management
Class II	Missed major diagnosis with no potential impact on survival that would not have changed therapy
Class III	Missed minor diagnosis related to terminal disease but not related to the cause of death
Class IV	Other missed minor diagnosis
Class V	Absolute agreement
Class VI	Uncertain autopsy diagnosis

Only a single category of discrepancy was assigned to each patient according to the most important type of disagreement. For instance, if a patient had one class IV diagnosis, one class III diagnosis and one class I diagnosis, the comparison would categorize this patient as a Goldman criteria class I.

Descriptive statistics were computed for all study variables. Numbers are shown as absolute numbers (percentages) or as the means \pm SDs (standard deviations). Binary regression analysis was performed to assess the impact of age, gender, length of stay in the hospital and main diagnosis on the concordant diagnosis.

RESULTS

From January 2003 to December 2006, 13.754 patients were admitted to the ICUs. Of these, 1504 (10.9%) patients died, and 98 (6.5%) patients underwent a postmortem examination. This number represents 23.2% of all autopsy requests during the study period, (medical ward: 23.2%, surgery ward: 7.2%, emergency department: 45.2%, gynecology and obstetrics: 0.4%). The mean age of the patients was 50.1 years. Patient characteristics according to the Goldman criteria are shown in table 2.

Five patients (5.1%) died within 24 hours of ICU admission, and 93 (94.9%) patients died more than one day after ICU admission. The postmortem examination

rates in ICU patients progressively declined over the study period. In 2003, autopsies were performed in 34.6% of cases; this number decreased to 30.6% in 2004, 19.3% in 2005, and 15.3% in 2006. This trend reflects a progressive decline in the overall rate of hospital postmortem examinations.

Forty-nine (50%) cases were classified as Goldman classes I and II, whereas 43 (43.8%) cases were class I, indicating that changes in management may have affected survival; in addition, 6 (6.1%) cases were Goldman class II, indicating that a change in therapy would not have changed survival (Table 3). In contrast, only 30 (30.6%) cases had complete agreement between premortem and postmortem diagnoses; these cases were categorized as

Table 2 - Characteristics of patients according to Goldman criteria

	Goldman I, II (Discordant) (N=49)	Goldman III, IV, V (Concordant) (N=37)	Goldman VI (Unknown) (N=12)	All patients (N=98)
Gender (male)	30 (61.2)	23 (62.1)	9 (75)	62 (63.2)
Age (years)	52.7 ± 13.8	46.0 ± 16.6	52.2 ± 17.8	50.1 ± 15.4
Hospital length of stay, days	11.0 ± 11.8	10.9 ± 13.0	5.2 ± 5.9	10.2 ± 11.8
Hospital length of stay <24 h	7 (14.2)	8 (21.6)	3 (25)	18 (18.4)

LOS: length of stay. The results are expressed as the number (%) and the mean ± standard deviation.

Table 3 - Pathological diagnosis and agreement between clinical and postmortem findings

Diagnosis	Discordant N=49	Concordant N=37	p value
Infections	17 (34.7)	20 (54.0)*	0.11
Pneumonia	10 (20.0)	12 (32.4)	0.30
Tuberculosis	1 (2.0)	3 (8.1)	0.41
Meningoencephalitis	1 (2.0)	2 (5.4)	0.79
Pyelonephritis	0 (0)	2 (5.4)	0.35
Pancreatitis	2 (4.0)	0 (0)	0.61
Enterocolitis	2 (4.0)	0 (0)	0.61
Endocarditis	0 (0)	1 (2.7)	0.88
Hernia	1 (2.0)	0 (0)	0.87
Cardiovascular causes	19 (36.7)	7 (21.6)	0.20
Acute myocardial infarction	8 (18.4)	4 (10.8)	0.50
Pulmonary thromboembolism	4 (8.1)	1 (2.7)	0.55
Cardiac heart failure/Cardiogenic shock	2 (4.0)	1 (2.7)	0.60
Enteromesenteric infarction	3 (6.1)	0 (0)	0.35
Cerebral vascular accident	1 (2.0)	1 (2.7)	0.61
Ruptured aorta aneurism	1 (2.0)	0 (0)	0.87
Post-operative complications	6 (12.2)	3 (8.1)	0.79
Hypovolemic shock	4 (8.1)	2 (5.4)	0.95
Liver failure	0 (0)	5 (13.5)	0.03
Acute pulmonary edema	3 (6.1)	0 (0)	0.35

Concordant: Goldman classes II, IV and V. Discordant: Goldman classes I and II.

*: p<0.05 vs. cardiovascular causes. The results are expressed as the number (%).

class V. Seven (7.1%) cases were categorized as correct diagnoses with only minor error classification ratings (classes III and IV) along with the class V diagnoses. There were 12 cases (12.2%) in which neither macroscopic nor microscopic examination could clarify the diagnosis; these cases were categorized as Goldman class VI (inconclusive) and were therefore not computed in table 3.

The main final events leading to death included septic shock in 37 patients (37.7%), cardiovascular events in 26 patients (26.5%; 12 cases of acute myocardial infarction, 5 cases of pulmonary thromboembolism, 2 cases of cerebral vascular accident, 3 cases of enteromesenteric infarction, 3 cases of cardiogenic shock and 1 ruptured aortic aneurism), post-operative complications in 9 patients (10,8%), hypovolemic shock in 6 patients (6,1%), acute pulmonary edema in 3 patients (3,1%) and liver failure in 5 patients (5,1%). Infections had a significantly greater rate of concordant diagnosis (49%) than cardiovascular diseases (26.2%) (p=0.002). Binary regression analysis revealed significant associations between a concordant diagnosis and both the diagnosis of infection (Odds Ratio (OR: 3.83 CI95% 1.19-12.3, p=0.025) and age (OR: 0.96 CI95% 0.93-0.99, p=0.02) (Table 4).

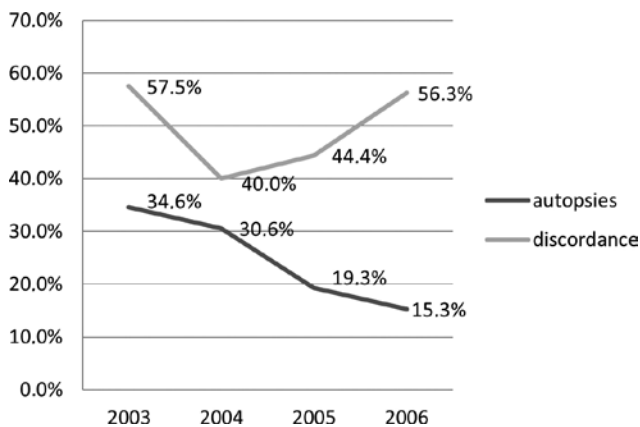


Figure 1 - Time-dependent analysis of the rates of autopsies and discordant diagnoses.

DISCUSSION

In this study, we evaluated clinicopathological diagnoses that originated from three ICUs of 40, 20 and 18 beds from a generalist tertiary care hospital. The autopsy rate in this institution is approximately 7%, which is far below the rate of 20% advocated by Valdez-Martinez, but this rate is consistent with the reports of decreasing autopsy rates worldwide.⁽⁹⁾

In countries with an autopsy-favorable legal system, such as Belgium, the autopsy rate can surpass 90%. The main reason for a low autopsy rate is family refusal.⁽¹³⁾ Other frequent alleged reasons include cost and an increased confidence in the performance of modern diagnostic techniques.⁽¹³⁾ According to McManus et al., autopsy rates have fallen for several reasons: clinicians may think that autopsies do not contribute with relevant information, medical students are poorly educated about autopsies and their benefits, pathologists have diminished interest in performing autopsies, clinicians fear medical litigation, physicians fear being wrong in either the diagnosis or the management of cases and pathologists lack financial incentives.⁽¹⁵⁾

We observed that in 50% of the patients, the diagnoses were categorized as Goldman classes I and II, revealing major discrepancies between clinical and pathological diagnoses. The rate of cases presenting concordance (Goldman classes III, IV and V) was approximately 38%. Previous studies have reported discrepancies (classes I and II) varying from 16% to 57%.^(9,10,12,16)

Comparing discrepancy rates from our heterogeneous population of critically ill patients with other published studies, we found similar or lower rates. In a similar population, Perkins et al. reported clinical-pathological discrepancies in 39% of cases.⁽¹²⁾ Kotovicz et al. reported a discrepancy rate of 16,3% in a population of 288 heterogeneous patients.⁽¹⁷⁾ Avgerinos-Bjornsson reported a rate of 17% for class I and II discrepancies in patients with malignancies.⁽¹⁸⁾ Jayawardena et al. evaluated patients in the emergency department and reported a discrepancy

Table 4 - Binary logistic regression for a concordant diagnosis

Factor	Regression coefficient	SE	OR	95% CI	p value
Gender (male)	0.2102	0.4850	0.81	0.31-2,10	0.66
Age (years)	-0.0373	0.0151	0.96	0.93-0.99	0.02
Diagnosis of infection	1.3440	0.5982	3.83	1.19-12.3	0.03
Diagnosis of cardiovascular cause	-0.3993	0.6827	0.67	0.18-2.56	0.55
Diagnosis of postoperative complication	-0.1479	0.8525	1.16	0.22-6.26	0.86
Hospital length of stay (days)	-0.001	0.0203	1.00	0.96-1.04	0.94

Log-Likelihood = -56.804. DF: 6. p value = 0.012. Goodness-of-Fit Tests: Hosmer-Lemeshow – Chi-squared: 15.25. p=0.05.

SE - standard error; OR – odds ratio; CI – confidence interval.

rate of 24.1%.⁽⁷⁾ In geriatric patients, a discrepancy rate of 52.5%⁽¹⁹⁾ was reported. In a subset of patients with cardiovascular diseases, a 29,9% discrepancy rate was found.⁽²⁰⁾ In a prospective study performed on patients who died in a university hospital medical-surgical ICU, autopsies revealed 171 missed diagnoses in 167 deaths, with Goldman classes I and II discrepancy rate of 32%.⁽¹³⁾

Older patients have a lower risk of diagnostic disagreement, which might be related to the fact that they usually die of predictable or already-diagnosed diseases. In our study, infections had a significantly higher rate of concordant diagnoses than cardiovascular diseases. In addition, a multivariate analysis identified that the likelihood of a concordant diagnosis were almost 4-fold higher for infections than for cardiovascular disease and revealed an inverse association between a diagnosis of cardiovascular disease and a concordant diagnosis. One possible explanation is that cardiovascular diseases, such as acute myocardial infarction, venous thromboembolism and mesenteric infarction, are much more difficult to diagnose in critically ill patients that may have many other confounding factors. Classical tests, such as troponin and D-dimer, are less useful in these situations. In addition, it is possible that general intensivists are better trained and have more tools to diagnose infections than cardiovascular diseases. Of greatest importance is the fact that in our institution, autopsies are performed only in cases of diagnostic uncertainty and not solely for academic purposes. In addition, many patients are referred to our ICU after prolonged stays in another department or hospital.

There are some limitations in our study that must be taken into account. First, our analysis is retrospective in nature; however, the data were collected prospectively. Second, this study included critically ill patients that were mainly suffering from surgical pathologies; thus, the results may not be applicable to other ICU populations. Third, the autopsy rate was low, and the reasons for refusal were

not known. Finally, the diagnosis could not be defined postmortem in 12.2% of cases.

CONCLUSION

This study identified significant discrepancies between clinical and pathological findings, reinforcing the value of postmortem examination, to clarify the terminal cause of death, to prevent future errors in diagnosis errors and to further medical education.

RESUMO

Introdução: A importância das autópsias é um tema comum de discussão tanto no Brasil como em todo o mundo, já que pode elucidar as causas de óbito e tem um valor social muito amplo. Entretanto, esta prática vem sendo gradualmente considerada desnecessária, tendo ocorrido um declínio no número de exames post-mortem.

Objetivos: Comparar o diagnóstico clínico e patológico em pacientes com difícil diagnóstico pre-mortem.

Métodos: Foram analisados todos os casos de autópsias (em um total de 98) de pacientes oriundos de três unidades de terapia intensiva médico-cirúrgicas (total de 78 leitos) pertencentes a uma faculdade de medicina, realizadas no período de janeiro de 2003 a dezembro de 2006. Analisamos os diagnósticos clínicos e patológicos segundo os critérios de Goldman.

Resultados: Em 49 casos (50%) foram encontradas discordâncias classes I e II de Goldman. Por outro lado, apenas 30 (30,6%) dos casos tiveram uma concordância completa entre os diagnósticos pre-mortem e post-mortem sendo classificados como classe V. As infecções tiveram uma taxa de concordância significativamente maior do que as doenças cardiovasculares.

Conclusão: Encontramos discrepâncias significantes entre os achados clínicos e patológicos, o que reforça o valor dos exames post-mortem.

Descritores: Autópsia; Diagnóstico clínico; Cuidados críticos

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