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Original contribution

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Summary We evaluate the evolution over time of discrepancies between clinical diagnoses and postmortem findings in critically ill patients and assess the factors associated with these discrepancies. We conducted a prospective study of all consecutive patients who underwent autopsy in a medical-surgical intensive care unit (ICU) between January 2008 and December 2015. Among 7655 patients admitted to our ICU, 671 (8.8%) died. Clinical autopsy was performed in 215 (32%) patients. Major missed diagnoses were noted in 38 patients (17.7%). Eighteen patients (8.4%) had class I discrepancies, and 20 patients (9.3%) had class II discrepancies. The most frequently missed diagnoses were invasive aspergillosis, intestinal ischemia, myocardial infarction, cancer, and intra-abdominal abscesses. We did not find a statistically significant correlation between any premortem factor, including age, sex, severity of illness, length of hospital stay before ICU admission, length of ICU stay before death, duration of mechanical ventilation, or admitting unit, and the level of agreement between clinical and pathological diagnosis. In the last decades, the discrepancies between clinical and autopsy diagnoses persisted despite advances in medical skills and technology. Specific clinical entities such as invasive aspergillosis, mesenteric ischemia, myocardial infarction, intra-abdominal abscesses, and neoplastic diseases remain a diagnostic challenge in critically ill patients. Clinical level of diagnostic certainty does not increase with specific premortem characteristics. © 2018 Elsevier Inc. All rights reserved.

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### 1. Introduction

Autopsy has long been regarded as a valuable and reliable tool in assuring and improving the quality of medical care by monitoring diagnostic accuracy and treatment of the critically ill patients. However, autopsy rates have been declining worldwide over the past few decades [1,2]. Studies comparing clinical diagnoses and autopsy findings have still frequently

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86 E. E. Tejerina et al.

found significant discrepancies. Major discrepancies have been reported in 10%-37% of all hospitalized patients [3,4], and in 7%-32% of adult intensive care patients, a treatable condition that might have altered outcome had it been recognized is identified at postmortem examination [5-13].

Although some authors reported a significantly reduced frequency of major discrepancies over time [14-17], others showed that, despite technological improvements in medicine, major discrepancy rates remained stable [2,18-20]. However, most studies included a case mix population, and the evolution over time of diagnostic errors in critically ill patients has been scarcely evaluated. On the other hand, risk predictors for misdiagnosis in the intensive care unit (ICU) are incompletely defined.

The objective of the present study was to evaluate the evolution of discrepancies between clinical diagnoses and postmortem findings over time in critically ill patients. The secondary objective was to assess the factors associated with these discrepancies.

#### 2. Materials and methods

We conducted a prospective study of all consecutive autopsies performed on patients who died in the ICU of the Hospital Universitario de Getafe, Madrid, Spain, between January 2008 and December 2015. We routinely approached the families and requested an autopsy for all patients who died, except those who became organ donors and those whose autopsies were legally mandated. The institutional ethics committee approved the study.

Clinical conditions were registered at ICU admission and during the length of ICU stay according to a problem-oriented record after agreement in daily clinical meetings. Final clinical diagnoses were established at the time of death. Medical records were reviewed by investigators who were blinded to the postmortem findings. Data collected included demographics, preexisting medical conditions, admitting service, need and days of mechanical ventilation, major clinical findings including the primary clinical disease, the presumed cause of death, and ICU length of stay.

We used a predefined protocol, described previously [5], for the pathologic examination and clinical-pathologic correlation. Postmortem study was performed within 12 hours of death. In the autopsy results, the pathologists also classified their findings as the underlying primary disease and the cause of death. Clinical and pathologic diagnoses were made independently and were only known at the end of the study to establish the differences in the diagnoses.

The clinical and pathologic diagnoses were classified according to the World Health Organization [20]. Underlying primary disease was the disease or injury that initiated the chain of morbid events directly leading to death. Cause of death was the lesion or functional disorder that was the direct cause of death, excluding the final events of a terminal illness. The diagnostic errors were classified in 2 categories using the Goldman criteria [18]. Class I errors were major misdiagnoses with direct impact on therapy. Class II diagnostic errors

comprised major unexpected findings that probably would not have changed therapy for any of the following reasons: the patient was already receiving appropriate therapy even though the diagnosis was not known; effective therapy was not available; or the patient refused further investigations or treatment. If there was disagreement between the reviewers about the presence of a diagnostic error, then 2 critical care physicians were consulted for an independent review.

#### 2.1. Statistical analysis

Data are expressed as mean (standard deviation [SD]), median (interquartile range [IR]), or proportion (95% confidence interval [CI]), as appropriate. We used  $\chi^2$  tests or Fisher exact test to compare categorical variables and a Student t test to compare mean values. All Ps are 2-sided, and a significance level of .05 was used for each hypothesis. A univariate analysis using Pearson  $\chi^2$  test was performed to investigate the relationship between specific characteristics (age, sex, severity of illness, duration of mechanical ventilation, length of hospital stay before ICU admission, length of ICU stay before death, and admission unit at the hospital) comparing with a discordant diagnosis. A logistic regression was developed to exclude residual confounding variables to determine both the odds ratio and the 95% CI.

### 3. Results

Among 7655 patients admitted to our ICU in the 8-year period, 671 (8.8%) died. A total of 70 organ donors and 50 patients with judicial autopsies were subsequently excluded (we did not have available data on judicial autopsies in 2008). Consent was obtained, and a clinical autopsy was performed in 215 of the remaining deaths. Refusal by the family was the most frequent reason for not performing an autopsy. Consequently, 215 (32%) were finally included. Autopsy rate showed some variation over the 8-year period (range from 25.7% to 47.4%) (Supplementary Figure).

Table 1 Baseline characteristics of deceased patients with autopsy n = 215Characteristics Age, mean (SD) 68 (13.7) 76 (35%) Sex, female, n (%) SAPS II, mean (SD) 63 (20.5) Length of ICU stay before death, median (IR) 2(1-11)Duration of mechanical ventilation before death, 2(1-10)median (IR) Length of hospital stay before death, median (IR) 8 (2-22) Last admission unit, n (%) Emergency department 81 (38) Medical wards 84 (39) Surgical wards 50 (23)

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