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Comparative validation of prognostic rules for community-acquired pneumonia in an elderly population

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Comparative validation of prognostic rules for community-acquired pneumonia in an elderly population. S. Ewig, T. Kleinfeld, T. Bauer, K. Seifert, H. Schäfer, N. Göke. ©ERS Journals Ltd 1999.

ABSTRACT: The aim of the study was to validate the prediction rule of M.J. Fine and coworkers for clinical outcome variables and three prognostic rules for the individual outcome of community-acquired pneumonia in an elderly population (rule 1: respiratory frequency ≥30 breaths·min^{-1}, diastolic blood pressure ≤60 mmHg, blood urea nitrogen >7 mM; rule 2: respiratory frequency ≥30 breaths·min^{-1}, diastolic blood pressure ≤60 mmHg, mental confusion; and rule 3: systolic blood pressure ≤80 mmHg, cardiac frequency ≥90 beats·min^{-1}, lactate dehydrogenase activity ≥260 IU·L^{-1}; death was predicted in the presence of at least two of three parameters).

Overall 168 consecutive episodes of community-acquired pneumonia in patients aged ≥65 yrs and hospitalized in a primary care hospital were studied prospectively. Fine's rule was tested for its ability to predict length of hospital stay, requirement for intensive care unit (ICU) admission and death. For the three prognostic rules of individual outcome, performance regarding predicting death was determined.

Mortality was 17/168 (10%). Fine's rule accurately predicted length of stay, the requirement for ICU admission and the risk of death from pneumonia as compared to the original derivation and validation cohorts. All three rules achieved moderate-to-high specificity (73%, 88% and 80%, respectively) and high negative predictive values (95%, 94% and 93%, respectively) but had a low sensitivity (65%, 47% and 47%, respectively). Rule 2 most closely reflected the risk of death from pneumonia when Fine's classification was used as reference.

Fine's rule proved to give valid estimations regarding clinical outcome variables of community-acquired pneumonia in the elderly. The prognostic rules may be useful in determining individual patients at lower risk of death caused by pneumonia.
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With an incidence of up to 30 cases per 1,000 inhabitants per year [1] and a mortality rate of 26–33% [2, 3], community-acquired pneumonia in the elderly remains a serious healthcare problem. This is even more true when demographic projections implying an increasing proportion of elderly persons in the general population are taken into account.

In order to ensure an appropriate identification of patients at risk of death caused by pneumonia, several prognostic rules for individual outcome have been suggested by the British Thoracic Society (BTS) [4] and by the authors [5]. Three validation studies of the BTS rules, in different settings, confirmed the potential of these rules in identifying patients at risk of death caused by pneumonia [6–8]. However, these rules were derived in general populations, and the BTS derivation study [4] as well as some of the validation studies of the BTS rules [7, 8] excluded part of the elderly population. Therefore, there remained concerns about the validity of these rules in community-acquired pneumonia in the elderly [9].

FINE *et al.* [10] developed a risk classification system based on age, sex, the presence of comorbid illnesses, vital sign abnormalities, and some laboratory and radiographic abnormalities, which permits estimation of the risk of death caused by pneumonia, as well as other important clinical outcome variables, in different subgroups. This predictive rule, although based on exceptionally large patient populations, has not as yet been validated prospectively in either in the general or the elderly population.

Therefore, a prospective study was conducted in a primary care hospital on the outcome of community-acquired pneumonia in the elderly in order to: 1) validate Fine's predictive rule for risk groups, 2) validate three prognostic rules for individual outcome, and 3) determine the predictive potential of these three rules for the estimation of patients at risk of adverse outcome using Fine's classification as reference.

Methods

The study was designed according to guidelines on investigations into the outcome of patients with community-acquired pneumonia, stressing the importance of properly defining the referral patterns, the inception cohort and follow-up of subjects [11].

Setting

The study was conducted at the Dreifaltigkeits-Krankenhaus Wesseling, which is a primary care hospital with ~200 beds. Wesseling (Germany) is a community located between Cologne and Bonn with ~35,000 inhabitants. The chemical industry represents the major employer. The Dept of Internal Medicine of this hospital does not include any speciality. No attempt was made to influence patient investigation or management, including decisions about antimicrobial treatment and admission to the intensive care unit (ICU).

Patient selection

All consecutive patients aged ≥65 yrs admitted between July 1, 1996 and March 31, 1998 with a diagnosis of community-acquired pneumonia on admission were prospectively documented. The diagnosis of community-acquired pneumonia was based on a new infiltrate on chest radiography, symptoms suggestive of a lower respiratory tract infection and no alternative diagnosis emerging during follow-up in a nonimmunosuppressed host not hospitalized during the previous month. Exclusion criteria were: 1) the presence of severe immunosuppression with inherent risk of opportunistic infections (human immunodeficiency virus infection, neutropenia ($<1 \times 10^9$ neutrophils·L^{-1}), and organ transplantation); 2) referral from another hospital after initiation of antimicrobial treatment; 3) gross aspiration; and 4) pulmonary tuberculosis.

Data collection

All data were recorded by two of the authors (T. Kleinfeld and K. Seifert) who were members of the staff of the Dept of Internal Medicine at the Dreifaltigkeits-Krankenhaus. On admission, the following demographic parameters were retrieved: age, sex, admission from home or nursing home, smoking habits and alcohol intake, comorbid illnesses, and previous oral corticosteroid treatment. Physical examination parameters included respiratory frequency, cardiac frequency, systolic and diastolic blood pressure, and mental confusion (defined according to FINE *et al.* [10] as "disorientation with respect to person, place or time that is not known to be chronic, stupor, or coma"). Laboratory parameters included leukocyte count, lactate dehydrogenase (LDH) activity, blood urea nitrogen, (BUN) haematocrit, and sodium and glucose concentrations. Further investigations included: blood gas analysis (pH, arterial oxygen concentration (P_{a,O_2}), arterial carbon dioxide tension, P_{a,O_2}/inspiratory oxygen fraction (F_{I,O_2}), extent and type of pulmonary infiltrates (uni- *versus* bilateral and alveolar *versus* bronchopneumonic) as well as the presence of pleural effusion. After discharge or death, the type of antimicrobial treatment, microbiological results and outcome variables (duration of hospitalization, requirement for ICU admission and for mechanical ventilation, survival or death within 30 days of hospital treatment) were also retrieved. Data were recorded on standard record sheets and entered into a computer database.

Calculation of prognostic rules

Patients were assigned to risk classes according to FINE *et al.* [10]. By definition, no patients fulfilled the criteria for risk class I (requiring age <50 yrs). For classification of individual outcome, nonsurvival was predicted if two or more of the following criteria in one rule were present on admission: 1) rule 1, as suggested by the BTS: respiratory frequency ≥30 breaths·min^{-1}, diastolic blood pressure ≤60 mmHg, BUN>7 mM [4]; 2) rule 2, as suggested by BTS: respiratory frequency ≥30 breaths·min^{-1}, diastolic blood pressure ≤60 mmHg, mental confusion [4] and 3) rule 3, as suggested by the authors in a previous study: systolic blood pressure ≤80 mmHg, cardiac frequency ≥90 beats·min^{-1}, LDH activity ≥260 U·L^{-1} [5]. Non survival was predicted by the presence of two of three variables and encoded "1".

Statistics

Results are expressed as mean±SD. Categorical variables were compared using the Chi-squared test or Fisher's exact test where appropriate. Comparisons of continuous variables of more than two groups were performed by one-way analysis of variance with *post hoc* Bonferroni correction. Performances of prognostic rules (sensitivity, specificity, and positive and negative predictive values) were assessed by means of standard formulae. The three components of each prognostic rule were entered into a multivariate stepwise forward logistic regression analysis in order to determine the independent prognostic weight of each variable. Finally, the rule of FINE *et al.* [10] was used as an additional reference for the prognostic rules in order to characterize their predictive potential in different risk classes. The level of significance was set at 5%.

Results

Patient population

Overall, 168 patients (66 males, 99 females, mean age 78±8 yrs) were included in the study. Two patients met exclusion criteria (referral from another hospital (n=1) and severe neutropenia (n=1)). The diagnosis of community-acquired pneumonia was found to be incorrect during follow-up in 11 cases. The main epidemiological and clinical characteristics of the study population are listed in table 1.

Clinical presentation at admission

Eighty-nine (53%) patients had a body temperature ≥38.3°C. At least one vital sign abnormality, as defined by FINE *et al.* [10], was present in 54 (32%) patients, including respiratory frequency ≥30 breaths·min^{-1} in 28 (17%), systolic blood pressure <90 mmHg in 5 (3%), cardiac frequency ≥125 beats·min^{-1} in eight (5%), mental confusion in 31 (19%) and body temperature ≥40°C in seven (4%) patients. Severe respiratory failure, as defined by $P_{a,O_2}/F_{I,O_2}$ <250, was present in 28 (17%) patients.

Table 1. – Epidemiological and clinical characteristics of 168 elderly patients with community-acquired pneumonia

Characteristic	n (%)
Age ≥75 yrs	108 (47)
Residence in nursing home	22 (13)
Previous hospitalization within last 2 yrs*	100 (60)
Previous pneumonia within last 2 yrs*	45 (27)
Current smoker**	42 (25)
Alcoholism***	4 (2)
At least one comorbid illness	156 (93)
One	39 (23)
Two	39 (23)
Three	30 (18)
Four	12 (7)
Comorbidity	
Cardiac	118 (70)
Hypertension	40 (24)
Pulmonary	56 (33)
Renal	21 (13)
Hepatic	1 (1)
CNS disorders	44 (26)
Diabetes mellitus	26 (16)
Neoplasia	21 (13)
Previous use of corticosteroids^{+}	7 (16)

*: not within the last month; **: ≥10 cigarettes·day^{-1}; ***: estimated intake ≥80 g alcohol·day^{-1}; $^{+}$: mainly for pulmonary disease. CNS: central nervous system.

Infiltrates on chest radiography were unilateral in 136 (81%) and bilateral in 32 (19%) patients, and were alveolar in 76 (45%) patients and bronchopneumonic in 88 (55%). Pleural effusion was present in 53 (32%) patients.

Aetiology

Only eight (5%) patients had a definite or probable microbial aetiology, including two patients with two pathogens. These pathogens included *Streptococcus pneumoniae* (n=2), *Staphylococcus aureus* (n=1), *Haemophilus influenzae* (n=1), *Klebsiella oxytoca* (n=2), *Enterobacter cloacae* (n=3), and *Morganella morgagnii* (n=1). Microbial diagnosis was based on blood culture (definite aetiology) and bronchoalveolar lavage (probable aetiology) in four cases each.

Antimicrobial treatment

Twenty-eight (17%) patients had antimicrobial treatment prior to hospital admission, with aminopenicillin (n=3), oral cephalosporins (n=4), macrolides (n=9), cotrimoxazole (n=2), tetracycline (n=8), and quinolones (n=2). Initial empirical inpatient treatment consisted of monotherapy in 122 (73%) and combination therapy in 46 (27%). Monotherapy included penicillins (n=90), first-generation cephalosporin (n=2), third-generation cephalosporin (n=6), macrolides (n=16) and quinolones (n=8). Combination therapy included penicillin plus aminoglycosides (n=14), penicillin plus quinolone (n=4), first-generation cephalosporin plus aminoglycosides (n=4), third-generation cephalosporin plus aminoglycosides (n=10), third-generation cephalosporin plus macrolide (n=3) and miscellaneous (n=11). Defervescence within 72 h after initiation of inpatient treatment was achieved in 70 of 89 (79%) patients with body temperature ≥38.3°C.

Outcome

Twenty-four (14%) patients were admitted to the ICU, but only four (2%) were intubated and mechanically ventilated. Seventeen (10%) patients died within 30 days after hospital admission. The mean hospitalization time of the whole population was 15±9 days (range 2–65), 16±9 days in survivors and 10±9 days in nonsurvivors ($p<0.01$).

Distribution of risk classes

All clinical, laboratory and radiographic data were complete except the following: cardiac frequency (n=1), mental confusion (n=1), BUN (n=1), sodium concentration (n=3), glucose concentration (n=4) and blood gas analysis (n=1) in eight (5%) patients. These missing values were regarded as zero points in the calculation of predictive rules.

The distribution of risk classes within the patient population and their related mortality rates and durations of hospitalization are given in table 2. One hundred and thirteen (67%) patients belonged to risk classes IV and V. No patient died in risk class II, 2.7% in risk class III, 7.5% in risk class IV, and 30.3% in risk class V. As regards ICU admission, 5.6% were admitted in risk class II, 10.8% in risk class III, 12.5% in risk class IV, and 27.3% in risk class V. The mean hospitalization time in survivors was significantly higher in risk classes IV and V compared to risk class II.

Validation of prognostic rules

The performances of the three prognostic rules are given in table 3. The relative risks (RR) of death caused by pneumonia were 4.1, 4.9, and 2.9, respectively. Although rule 1 had the greatest sensitivity (65%), rule 2 was most specific (88%). Rule 3 had intermediate performances (sensitivity 47%, specificity 80%).

As regards the parameters of rule 1, a respiratory frequency ≥30 breaths·min^{-1} had a high specificity (87%). BUN >7 mM had a high sensitivity (88%) but low specificity (44%) for death. This performance did not change when 21 patients with pre-existing renal disease

Table 2. – Classification of the patient population*

Risk class	Patients n (%)	Duration of hospital stay in survivors/all days	Nonsurvivors n (%)	Admission to the ICU n (%)
I	Absent by definition**			
II	18 (10.7)	9.6/9.6	0	1 (5.6)
III	37 (22.0)	14.9/14.7	1 (2.7)	4 (10.8)
IV	80 (47.6)	16.6^{+}/15.9$^{\#}$	6 (7.5)	10 (12.5)
V	33 (19.6)	19.1^{+}/16.2	10 (30.3)	9 (27.3)

*: according to the rule of FINE *et al*. [10]; **: risk class I requires age <50 yrs. ICU: intensive care unit. $^{+}$: p=0.005; $^{\#}$: p=0.039, compared to risk class II (calculated by one-way analysis of variance with *post hoc* Bonferroni correction).

Table 3. – Performance of three prognostic rules regarding death caused by community-acquired pneumonia

Performance	Rule 1	Rule 2	Rule 3
Sensitivity n (%)	11/17 (65)	8/17 (47)	8/17 (47)
Specificity n (%)	110/151 (73)	133/151 (88)	120/151 (80)
Positive predictive value n (%)	11/52 (21)	8/26 (31)	8/39 (21)
Negative predictive value n (%)	110/116 (95)	133/142 (94)	120/129 (93)
Overall accuracy n (%)	121/168 (72)	141/168 (84)	128/168 (76)
Relative risk (95% CI)	4.1 (1.6–10.5)	4.9 (2.1–11.4)	2.9 (1.2–7.1)

Patients were classified as nonsurvivors as described in Calculation of prognostic rules section. Sensitivity: correctly classified nonsurvivors/total number of nonsurvivors; Specificity: correctly classified survivors/total number of survivors; Positive predictive value: correctly classified nonsurvivors/total number of patients classified as nonsurvivors (correct plus false positive); Negative predictive value: correctly classified survivors/total number of patients classified as survivors (correct plus false negative); Overall accuracy: correctly classified nonsurvivors and survivors/total number of patients; CI: confidence interval.

were excluded (sensitivity 85%, specificity 48%). The presence of a diastolic blood pressure ≤60 mmHg was neither sensitive nor specific (table 4). Accordingly, only respiratory frequency ≥30 breaths·min^{-1} (RR 5.6, 95% confidence interval (CI) 1.9–16.9, p=0.002) and BUN >7 mM (RR 5.4, 95% CI 1.2–24.9, p=0.032) were independently associated with death on multivariate analysis.

The presence of mental confusion was specific for death caused by pneumonia (87%) (table 4). On multivariate analysis including the three parameters of rule 2, both respiratory frequency ≥30 breaths·min^{-1} (RR 3.5, 95% CI 1.1–11.3, p=0.032) and mental confusion (RR 6.5, 95% CI 2.1–19.9, p=0.001) proved to be factors independently associated with death.

The presence of a systolic blood pressure ≤80 mmHg was highly specific (99%) for death caused by pneumonia, whereas an LDH activity ≥260 U·L^{-1} had a moderate specificity (74%). A cardiac frequency ≥90 beats·min^{-1} was moderately sensitive but not specific (table 4). Correspondingly, only systolic blood pressure ≤80 mmHg (RR 12.8, 95% CI 1.8–90.7, p=0.01) and LDH activity ≥260 U·L^{-1} (RR 3.5, 95% CI 1.2–10.3, p=0.02) were independently associated with death on multivariate analysis.

The assignment of the prediction made by the three prognostic rules into the risk classes of FINE *et al.* [10] is given in table 5. All three rules achieved a remarkable approximation to the risk of death when Fine′s classification was used as reference, especially in risk classes IV and V. Nevertheless, significant differences between proportions of observed and predicted nonsurvivors were obvious for risk classes III–V when applying rule 1, risk class V when applying rule 2, and risk classes III and IV when applying rule 3. Overall, rule 2 achieved the closest approximation to the risk of death according to Fine′s classification.

Table 4. – Performances of single parameters of the three prognostic rules*

	Sensitivity n (%)	Specificity n (%)
Rule 1		
Respiratory frequency ≥30 breaths·min^{-1}	8/17 (47)	131/151 (87)
Diastolic blood pressure ≤60 mmHg	8/17 (47)	102/151 (68)
Blood urea nitrogen >7 mM	15/17 (88)	66/150 (44)
Rule 2**		
Mental confusion	10/17 (59)	130/150 (87)
Rule 3		
Systolic blood pressure ≤80 mmHg	3/17 (18)	149/151 (99)
Heart rate ≥90 beats·min^{-1}	12/17 (71)	64/150 (43)
LDH ≥260 U·L^{-1}	10/17 (59)	111/151 (74)

*: the sensitivity and specificity of the prognostic rules are shown in table 3 and sensitivity and specificity defined in the legend to that table; **: respiratory frequency and diastolic blood pressure as rule 1. LDH: lactate dehydrogenase.

Discussion

This study provides three important results with regard to the prediction of outcome in hospitalized elderly patients with community-acquired pneumonia. 1) Fine′s classification provided an accurate estimate of the risk of death caused by community-acquired pneumonia and the requirement for ICU admission. Moreover, risk classes were closely related to the duration of hospital stay. 2) All three prognostic rules for individual outcome were associated with comparable RRs for death (2.9–4.9) and equally high negative predictive values (93–95%); however, sensitivity remained low (47–65%). Diastolic blood pressure ≤60 mmHg and cardiac frequency ≥90 beats·min^{-1} were identified as invalid prognostic parameters. 3) The second rule of the BTS (respiratory frequency ≥30 breaths·min^{-1}, diastolic blood pressure ≤60 mmHg and mental confusion) provided the best approximation to the risk of death caused by pneumonia when Fine′s classification was used as reference.

The case definition of pneumonia is made difficult by the fact that there is no precise consensus as to which criteria are essential for the diagnosis of pneumonia [12]. The present study population had a high mean age of 78±8 yrs including 47% patients aged >75 yrs (representing the "very elderly"). Moreover, 93% had at least one comorbid illness, with cardiac illnesses representing by far the most frequent one (70%). Roughly half (47%) of the population presented with apyrexia. Finally, since the general policy of the Department of Internal Medicine was to treat empirically and to restrict microbial investigation to patients with fever and chills or nonresponding episodes and not to rely on sputum cultures, the proportion of episodes with an aetiological diagnosis remained very low (5%). Despite these potential diagnostic confounders, the following facts should be recognized. First, common clinical and radiographic criteria, applied in many other epidemiological series on community-acquired pneumonia, were used. Alternative approaches requiring a proportion of a set of clinical criteria remain arbitrary because of a lack of validation. Secondly, the proportion of apyrexia was very comparable to the

Table 5. – Assignment of the prediction made by the three prognostic rules into risk classes[+]

Risk class[+]	Patients n	Observed nonsurvivors n (%)	Rule 1		Rule 2		Rule 3	
			Predicted nonsurvivors n (%)	Difference (95% CI)[#]	Predicted nonsurvivors n (%)	Difference (95% CI)[#]	Predicted nonsurvivors n (%)	Difference (95% CI)[#]
I	0		Absent by definition[‡]					
II	18	0	1 (5.6)	5.6 (-5.0–16.2)	0	0	0	0
III	37	1 (2.7)	8 (21.1)	18.4 (4.3–32.6)*	0	2.7 (-2.5–7.9)	7 (18.4)	15.7 (2.2–29.2)*
IV	80	6 (7.5)	24 (30.4)	22.9 (11.3–34.5)*	8 (10.1)	2.6 (-6.2–11.4)	20 (25.3)	17.8 (6.7–28.9)*
V	33	10 (30.3)	19 (57.6)	27.3 (4.3–50.3)*	18 (54.5)	24.2 (1.1–47.3)*	12 (36.4)	6.1 (-16.6–28.8)

[+]: of FINE *et al.* [10]; [#]: between observed and predicted nonsurvival rate; [‡]: risk class I requires age <50 yrs. CI: confidence interval. *: $p<0.05$.

41% found by others [3]. Thirdly, it is generally held as true that microbiological confirmation of the diagnosis of pneumonia is not necessary in community-acquired pneumonia [12]. It is also known that an aetiological diagnosis can only be made in ≤50% of cases, even in most prospective epidemiological series. However, additional efforts were made to validate the diagnosis of community-acquired pneumonia by means of introducing clinical follow-up as a further strong *post hoc* diagnostic criterion. Strict exclusion criteria, especially for severely immunosuppressed patients, were also applied. Therefore, arguably, the standards for the diagnosis of community-acquired pneumonia were at least comparable to those used in other studies [2, 3, 5–8].

The prediction rule of FINE *et al.* [10] was originally designed to identify patients at low risk who can be safely treated as outpatients. Therefore, it did not provide a rule for predicting individual outcome but for estimating the risk of death caused by community-acquired pneumonia in a given risk class. To the author′s knowledge, the present study is the first to prospectively validate this classification system in an elderly population. The risks of death caused by pneumonia in risk classes II–V were very similar to those reported for the Medis Group and inpatient Port validation cohorts [10] (0, 2.7, 7.5, and 30.3% as compared to 0.6, 2.8, 8.2, and 29.2 and 0.9, 1.2, 9.0, and 27.1%, respectively). Fine′s risk classes were also closely related to the risk of requirement of ICU admission. The risks of ICU admission in risk classes II–V were 5.6, 10.8, 12.5 and 27.3%, respectively, as compared to 4.3, 5.9, 11.4 and 17.3% in the Port cohort. Finally, although the duration of hospital stay was considerably longer in the present population than in the Port cohort (mean duration of hospitalization in this study 15 days *versus* 7 days in the Port cohort), in accordance with the Port cohort, the duration of hospital stay in survivors was significantly longer in risk classes IV and V as compared to risk class II. Thus, Fine′s classification also proved an accurate predictive classification for important clinical outcome variables in the present elderly population.

The fact that the mortality rate was at the lower range of that expected (10%) is most probably due to the population having relatively low proportions of risk classes IV and V, since mortality rates in each risk class were almost exactly those predicted by Fine′s score. This may in turn be explained by the fact that the study was conducted in a primary care hospital; attending physicians may have refered the more severely ill to one of two tertiary care settings in the near neighbourhood (University of Bonn or Cologne).

In addition to Fine′s rule, three different rules were derived by the BTS and the present authors to predict the individual outcome of an episode of community-acquired pneumonia. All three of these rules had so far not been validated in an elderly population. Moreover, the BTS derivation study had excluded patients aged >74 yrs. Although BTS rule 2 gave results very similar to the derivation and one validation study (sensitivity 47% and specificity 88% in the present series compared to 39 and 94% in the derivation study [4] and 35 and 89% in the validation study [7], respectively), BTS rule 1 failed to achieve the favourable performances reported in the derivation and two validation studies (sensitivity 65% and specificity 73% compared to 88 and 79% in the derivation study [4] and 70 and 84% [7] as well as 90 and 76% [8] in two validation studies, respectively). As regards the third rule, specificity was close to that reported in the derivation study (80% compared to 77%), but specificity achieved only 47% as compared to 77% in the derivation study [5]. These results suggest that rule 2 is the one that may most appropriately be applied to the elderly.

An analysis of the performance of single parameters of these three rules revealed that a respiratory frequency ≥30 breaths·min^{-1}, BUN >7 mM, mental confusion, systolic blood pressure ≤80 mmHg and LDH activity ≥260 U·L^{-1} were the parameters with favourable operative indices and independently associated with death when the parameters of each rule were entered into multivariate analysis. These results confirm previous findings [4, 5, 13–15]. Moreover, LDH activity was confirmed as an adverse prognostic factor [5]. Conversely, the parameters diastolic blood pressure ≤60 mmHg and cardiac frequency ≥90 beats·min^{-1} were neither sensitive nor specific. Since cardiac illnesses were by far the most frequent comorbid illnesses, affecting 70% of the whole population, their inadequate performance, especially of cardiac frequency, may be explained by a high prevalence of autonomic dysregulation or arrhythmias. The failure of diastolic blood pressure to contribute to the prognostic prediction, in contrast to systolic hypotension, may also be related to difficulties in correctly assessing diastolic arterial pressure by means of the Riva-Rocci method, as already outlined previously [5]. As regards BUN, it should be noted that despite its excellent sensitivity and independent contribution to the prediction of mortality within the

parameters of rule 1, specificity remained low. This finding confirms concerns about the validity of BUN in the elderly, in whom an elevated BUN may be more prevalent or at least more readily develop [9]. Although an elevated BUN may be falsely positive in patients with pre-existing renal disease (which was present in 13% of the present population), this potential confounder did not account for the lack of specificity in this series. Conversely, mental confusion was highly specific and also proved to be independently associated with death on multivariate analysis of parameters included in rule 2. Thus, the analysis of single parameters included in the three prognostic rules supports the conclusion that a prognostic rule in an elderly population should incorporate mental confusion rather than BUN.

Finally, this view is also supported by the application of the three prognostic rules for the individual outcome as rules for the prediction of the risk of death within the risk groups of Fine′s classification. Rule 2 proved to provide the closest approximation to the risk of death as given by Fine′s classification.

In conclusion, although Fine′s rule proved to represent an excellent predictive rule for important clinical outcome variables, which might be applied in clinical research as well as for the purposes of quality control, the three predictive rules for individual outcome can only serve as an adjunct to clinical judgment. The present data indicate that, at least in the elderly, these rules may be useful in clinical practice, relying primarily on their negative predictive potential, *i.e.* in identifying the patients at lower risk. The second British Thoracic Society rule, including mental confusion, may most accurately identify patients at risk of death.

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