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Risk Factors Associated with Adverse Drug Reactions Following Hospital Admission

A Prospective Analysis of 907 Patients in Two German University Hospitals

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Abstract

Background: Since the 1970s, studies have examined potential risk factors associated with adverse drug reactions (ADRs) in a variety of settings. However, no pharmacoepidemiological study exists that incorporates clinical and laboratory parameters in a multiple regression model in order to consider predictors for ADRs.

Objectives: To characterize risk factors associated with ADRs in patients admitted to university hospital departments of internal medicine.

Design and Setting: Intensive pharmacovigilance was carried out in departments of internal medicine of two university hospitals. All admissions were followed prospectively for the occurrence of ADRs by members of a pharmacoepidemiological team consisting of physicians, pharmacologists and pharmacists. To identify patients at high risk for experiencing ADRs, patient histories and several clinical and laboratory data, determined at the time of admission, were taken into consideration. In addition to the drug prescribed, 40 parameters defined vital status at admission. These included temperature, heart rate, blood pressure (systolic-diastolic), body mass index, nicotine and alcohol use, and first laboratory test results after admission on nutrition status, inflammation, liver, kidney, pancreas or thyroid status, electrolytes, blood count and coagulation.

Results: 907 patients were observed during the study period. The mean age of the study population was 60 ± 16 years. The median number of different drugs administered per patient during hospitalization was 9.6 ± 7.7. In 345 patients, 592 ADRs were evaluated: 33.4% possible, 61.5% probable and 4.7% highly probable. Two ADR-related deaths were observed during the study period. Analysing ADR predictors, 17 of 40 parameters reached significance in univariate analysis, but only five in a multivariate binary regression model: raised temperature (odds ratio [OR] 1.609; 95% CI 1.133, 2.285), low erythrocyte levels (OR 0.386; 95% CI 0.194, 0.768), low thrombocyte levels (OR 0.788, 95% CI 0.627, 0.989), high

number of drugs (OR 1.117; 95% CI 1.076, 1.159) and female sex (OR 1.562; 95% CI 0.785, 2.013) were independent predictors for ADRs.
Conclusion: For the patients investigated, of the large number of clinical data available only five independent factors predict ADR occurrence. Taking these results into account, physicians will be able to focus early on patients at risk for ADRs. To minimize ADR occurrence, ADR predictors should be integrated into the clinical pathway.

Background

Many investigators have analysed the characteristics and outcome of adverse drug reactions (ADRs), e.g. morbidity and mortality.[1-40] Individuals in the community experiencing ADRs, hospital admissions due to ADRs and inpatients experiencing ADRs affect our healthcare systems.[9,26,41] This highlights the need for ADR prevention strategies to be established in clinical practice.

Since the 1970s, the results of epidemiological studies exploring the relationship between age, polypharmacy, multiple morbidity, sex, organ dysfunction and ADRs have been diverse and are still under discussion.[5,6,8,9,22,30,33] Furthermore, for three decades it has been known that chemotherapeutic agents, cardiac drugs, anti-infective agents and antipsychotic medications are responsible for most of the severe ADRs. The resulting ADRs, including arrhythmia, bleeding, heart failure or allergic and dermatological symptoms, are well documented.[4,24,33]

Despite the implementation of pharmacovigilance systems, which in most cases analyse ADRs retrospectively, neither the prevalence of ADRs nor their consequences have decreased.[6,9,12,19,20,32,33,42] The newly emerging field of phenomics (studies concerned with the interaction of the genome with the environment) might offer solutions to the individual prediction and decreasing the risk for ADRs; but systems based on these approaches are not expected to become available to the practicing clinician in the near future.[43,44]

In contrast, at present, individual ADR predictors could be considered, and used in clinical practice, based on the increasing amount of data (e.g. laboratory data, diagnosis, drugs administered, patient characteristics) automatically available in hospital information systems.

The aim of this study was to characterize risk factors associated with ADRs during hospital admission.

Methods

Study Design

All admissions to two university hospital departments of internal medicine in Regensburg and Erlangen (Germany) underwent intensive pharmacovigilance by three physicians, one pharmacologist and three pharmacists, who were trained during former pharmocovigilance projects. Patient charts were screened and bedside visits were completed on a daily basis by a pharmacoepidemiological team (PETE) consisting of one physician and one pharmacist for detection and evaluation of potential ADRs. If there was disagreement after both had evaluated ADRs, a third physician, pharmacist or pharmacologist arbitrated until they reached consensus.

In addition to all information available from the hospital information system (demographic data, diagnoses classified according the International Classification of Disease – 10th Revision [ICD 10], and according to the German Diagnosis-Related Group (DRG)[45] laboratory data, investigations, medical history, etc.), evaluated information on ADRs (probability, severity, and preventability), their causative drugs and therapeutic consequences were stored in a specially developed database, KLASSE.[46]

Patient Characteristics

In addition to the generally evaluated parameters mentioned above, the physical status, alcohol and nicotine use, laboratory values and vital signs (temperature, heart rate and blood pressure) of patients were recorded.

Alcohol and nicotine use were categorized as abstinence from alcohol, current moderate alcohol consumption (female <20 g/day; male <40 g/day) and heavy alcohol consumption (female >20 g/day; male >40 g/day). Since the second and third categories did not differ in terms of ADR probability, they were merged. Nicotine use was categorized as non-use, moderate use (<10 cigarettes per day) and heavy use (>10 cigarettes per day).

Of 3421 different laboratory tests available at the laboratories of the two universities, 323 nominal tests were determined during the study period, and of these 323 laboratory tests the most commonly analysed parameters represented the following organ systems: liver (alkaline phosphatase U/L, γ-glutamyl transpeptidase U/L, AST U/L, ALT U/L), kidney (urea mg/dL, creatinine mg/dL, uric acid mg/dL), pancreas (amylase U/L, lipase U/L), thyroid (thyroid-stimulating hormone μE/mL), and blood count (erythrocyte $\times 10^6$/μL, leukocyte $\times 10^3$/μL, thrombocyte $\times 10^6$/μL, haematocrit %, haemoglobin g/dL, mean cell volume fL eosinophils %, monocytes %, lymphocytes %). Parameters describing the nutritional status (albumin g/L, protein g/L, triglyceride mg/dL, glucose mg/dL, serum iron μg/dL), inflammation (cholinesterase U/L, C-reactive protein [CRP] mg/L), electrolytes (calcium mmol/L, potassium mmol/L, sodium mmol/L) and coagulation (prothrombin time) were also included.

Classification of Drugs

For classification of drug prescriptions, the Anatomical Therapeutic Chemical Classification (ATC) System was used. It is controlled by the WHO Collaborating Centre for Drug Statistics Methodology, and was first published in 1976. The classification system divides drugs into different groups according to the organ or system on which they act and their therapeutic and chemical characteristics.[47]

Characteristics of Adverse Drug Reactions (ADRs)

Definition

Adverse drug reactions were defined according to the Adverse Reaction Terminology of the WHO definition: "A response to a drug which is noxious and unintended, and which occurs at doses normally used in man for the prophylaxis, diagnosis, or therapy of disease, or for the modification of physiologic function."[48]

Probability

The probability of ADRs was evaluated by the PETE using the Naranjo score algorithm. Doubtful ADRs were excluded from statistical consideration.[49]

Severity

The PETE assigned the severity of each ADR according to the Common Toxicity Criteria (CTC),[50] which provides descriptive terminology for adverse event reporting. A grading (severity) scale is provided for each adverse event term. CTC contains 24 categories organized by pathophysiology and anatomy. Grades were defined using a 0–5 scale, with 0 representing 'no adverse event' and 5 representing 'death related to adverse event'.

Type and Outcome of ADRs

ADRs were also classified according to the WHO Adverse Drug Reaction terminology (WHO-ART) into six types: (i) 'dose-related'; (ii) 'non-dose-related'; (iii) 'dose- and time-related'; (iv) 'time-related'; (v) 'failure of therapy'; and (vi) 'adverse reactions by withdrawal'.

Outcomes were classified according to the method of the German Federal Institute for Drugs and Medical Devices 'Bundesinstitut für Arzneimittel und Medizinprodukte'.[5] The outcome of each ADR was categorized into one of the five groups as follows: 'recovered', 'outcome unknown at discharge', 'not resolved during hospitalization', 'persistent' and 'death'.

Because some patients had several ADRs simultaneously or successively, the total number of reactions is greater than the total number of patients

having a reaction. If more than one drug was suspected of contributing to an ADR, the most likely drug was used for analysis and statistics.

Statistical Methods

Descriptive statistical methods were applied first. We used the t-test or Wilcoxon's rank test for continuously distributed variables and the chi-square test for categorical variables.

Univariate and multiple logistic regression models were constructed using ADR as the outcome using SAS® software (SAS Institute Inc., Cary, NC, USA).

The Bonferroni correction was applied for the multiple testing of problems.

Correlations between potential risk factors were assessed, and any highly correlated variables were analysed in separate models. Age and sex were used in all models.

We calculated odds ratios from the logistic regression with 95% confidence intervals. The ability to predict an ADR by different models was assessed with receiver operating characteristic (ROC) analyses. Therefore, predicted probabilities were estimated from the model equation and the sensitivity was plotted versus 1- specificity for all possible cut-off points to classify patients into ADR-positive and ADR-negative patients.

Results

During a 6-month study period in two university hospitals, 907 patients were intensively monitored with respect to ADRs. The mean length of hospital stay was 8.6 days (SD ± 9.4; minimum 1 day, maximum 91 days).

Patient Characteristics

Age and Sex

Mean age of the study population was 60 ± 16 years (16–94 years), comprising 480 males and 423 females.

Vital Signs on Admission

The mean systolic blood pressure was 127 ± 22 mmHg and diastolic 74 ± 12 mmHg. The mean body temperature was 37 ± 0.7°C and heart rate 78 ± 14 beats/min. The mean body mass index (BMI) was 25 ± 5 kg/m^2.

History of Nicotine and Alcohol Use

Of the patients, 408 (45.0%) declared they had never smoked. About 9.4% reported moderate smoking (<10 cigarettes/day) and 9.6% heavy smoking (>10 cigarettes/day). A total of 15.2% had smoked in the past.

In addition, 292 (32.1%) of the patients reported that they do not use alcohol. A moderate consumption of alcohol was reported by 28.9% and heavy consumption by 7.3% of the patients; 5.9% stated that they had consumed alcohol in the past.

No data were available on alcohol or tobacco use in 233 (26%) and 190 (12%) patients, respectively.

Diagnosis-Related Group

The distribution of patients according to DRG resulted in diseases of the alimentary tract 33.6% (n = 305), hepatobilliary/pancreatic system 24.9% (n = 226), pulmonary system 10.2% (n = 93), metabolic system 5.2% (n = 47), cardiopulmonary system 4.3% (n = 39), musculoskeletal disorders 3.0% (n = 27) and intoxication 2.9% (n = 26) and others 15.9% (n = 144).

Initial Laboratory Tests after Admission

Tests were performed in nine different categories: inflammation, electrolytes, blood count, coagulation parameters, and nutritional, liver, pancreatic, thyroid and renal status (table I).

Drugs

The mean number of different drugs administered per patient during hospitalization was 16.8 ± 8.7 (median 16.0) and 9.2 ± 6.4 (median 8.0) for ADR-positive and ADR-negative patients, respectively.

ADR Characteristics: Probability, Type, Outcome, Severity

The ADR rate among the patients was 38% (n = 345). The total number of ADRs was 592 (33.4% possible, 61.5% probable and 4.7% highly probable ADRs).

Table I. Differences in mean values of 31 laboratory test results in adverse drug reaction (ADR)-positive and ADR-negative patients

Parameter	Laboratory test [n (%)][a]	ADR-positive (mean ± SD)	ADR-negative (mean ± SD)	p-Value
Nutrition	Albumin [674 (40.4)]	36.2 ± 8.8	40.0 ± 6.7	<0.0001[b]
	Protein [578 (38.8)]	64.6 ± 9.5	69.8 ± 7.0	<0.0001[b]
	Triglyceride [523 (38)]	123.8 ± 56.5	124.4 ± 68	0.5098
	Glucose [705 (39)]	118.0 ± 43.6	112.7 ± 41.6	0.0127
	Serum iron [513 (38.8)]	71.1 ± 51	83.7 ± 47.9	0.0002[b]
Inflammation	Cholinesterase [535 (38.7)]	556.0 ± 1643	492.0 ± 1810	0.0004[b]
	CRP [615 (46.8)]	44.6 ± 64.3	27.5 ± 43.9	<0.0001[b]
Liver status	AP [798 (39)]	175.0 ± 280	111 ± 167	<0.0001[b]
	γGT [711 (39)]	217.0 ± 365.6	156.0 ± 450	<0.0001[b]
	AST [782 (40)]	60.9 ± 93	45.6 ± 76.6	<0.0001[b]
	ALT [785 (39.6)]	64 ± 127.8	54.7 ± 142	0.0046
	Bilirubin [803 (39.2)]	1.47 ± 3.1	1.0 ± 1.8	0.0056
Electrolytes	Calcium [678 (40)]	2.22 ± 0.2	2.3 ± 0.15	<0.0001[b]
	Potassium [850 (39.8)]	4.2 ± 0.5	4.3 ± 0.4	0.0019
	Sodium [848 (39.9)]	137.6 ± 3.9	138.5 ± 3.1	<0.0001[b]
Renal status	Urea [745 (39.7)]	46.3 ± 32.2	34.5 ± 17.7	<0.0001[b]
	Creatinine [852 (39.9)]	1.1 ± 0.7	0.9 ± 0.5	0.5963
	Uric acid [645 (39.7)]	5.4 ± 2.4	5.0 ± 1.7	0.3709
Pancreas status	Amylase [613 (37.8)]	53.2 ± 29.2	60.0 ± 6.7	0.0401
	Lipase [578 (38.1)]	43.9 ± 39.8	48.7 ± 56.9	0.2766
Blood count	Erythrocyte [870 (39.5)]	3.9 ± 0.7	4.3 ± 0.7	<0.0001[b]
	Leukocytes [871 (39.5)]	7.9 ± 4.3	7.5 ± 3.9	0.6646
	Thrombocytes [870 (39.5)]	240.0 ± 115	251.0 ± 94.6	0.0013[b]
	Haematocrit [870 (39.5)]	35.0 ± 6.4	39.0 ± 5.5	<0.0001[b]
	Haemoglobin [870 (39.5)]	11.9 ± 2.1	13.3 ± 1.9	<0.0001[b]
	MCV [870 (39.5)]	90.5 ± 6.5	89.6 ± 5.7	0.1565
	Eosinophils [365 (44)]	1.75 ± 1.79	2.2 ± 2.6	0.1504
	Monocyte [368 (43)]	6.0 ± 3.6	6.7 ± 2.9	0.0041
	Lymphocyte [351 (44.5)]	18.7 ± 11.5	24.1 ± 12.2	<0.0001[b]
Coagulation	Prothrombin time [585 (42.7)]	78.5 ± 19.1	85.8 ± 13.3	<0.0001[b]
Thyroid status	TSH (267 [45.7])	2.1 ± 3.3	1.5 ± 1.9	0.0037

a n = total number of patients who were tested for each parameter and the number of patients who were ADR-positive (%).

b Bonferroni corrected $p < 0.00163$.

γGT = γ-glutamyl transpeptidase; **AP** = alkaline phosphatase; **CRP** = C-reactive protein; **MCV** = mean cell volume; **TSH** = thyroid-stimulating hormone.

ADRs were also classified according to WHO-ART into six types.[48] The most commonly observed in the current study were: dose-related reactions (n = 281; 47.5%), non-dose-related (n = 103; 17.4%) and dose- and time-related (n = 167; 28.2%), followed by time-related (n = 38; 6.4%) and failure of therapy in three cases (0.5%). Adverse reactions resulting from drug withdrawal were not seen.

The outcome of each ADR, as categorized during hospitalization was: 'recovery achieved' in 226 (38.2%) ADRs. Due to the short duration of hospital stay in 184 (31.1%) cases, the 'outcome was unknown' at discharge. In 163 (27.5%), the ADRs had 'still not resolved' and 17 (2.9%) ADRs were assessed as 'persistent'. Most of the ADRs were of mild (n = 314; 53.0%) or moderate (n = 161; 27.2%) severity. Eighty-four ADRs (14.2%) were severe and 17 (2.9%) were life-threatening or disabling. Two ADR-related deaths (0.2%) were observed during the study period.

Table II. Results of the multivariate analysis for the occurrence of adverse drug reactions, including alcohol consumption. Estimates are additionally adjusted for age, heart rate, hospital stay, department effect and laboratory

Predictors	Odds ratio (95% CI)	p-Value
Sex	1.257 (0.785, 2.013)	0.3414
Body temperature	1.609 (1.133, 2.285)	0.0079
Erythrocyte count	0.386 (0.194, 0.768)	0.0067
Thrombocyte count	0.788 (0.627, 0.989)	0.0403
No. of drugs	1.117 (1.076, 1.159)	<0.0001
Alcohol	2.049 (1.228, 3.258)	0.0024

Patient Characteristics as a Predictor for ADRs

Univariate Analysis

Basic Demographics

In the univariate analysis, the influence of basic demographic variables – including age and sex, vital signs at admission, and tobacco and alcohol consumption – on the occurrence of ADRs is summarized in table II.

First Laboratory Test Results after Admission

Seventeen of 31 investigated laboratory tests showed a significant association with the occurrence of ADRs (Bonferroni corrected $p < 0.0016$).

Poor nutritional status, represented by lower albumin, protein and iron deficiency, predisposed to a higher ADR incidence in the study population. Elevated CRP as an indicator for inflammatory diseases, elevated liver enzymes and reduced coagulation all showed a significant relationship to ADRs.

Elevated blood urea nitrogen was associated with the occurrence of ADRs, but pathological values of uric acid or creatinine did not increase the ADR risk. An increased ADR rate was also seen for low pathological levels of electrolytes, decreased erythrocytes, low platelet count and low lymphocytes. Further details of laboratory test results are shown in table I.

Drugs

Polypharmacy was found to predispose patients to ADRs. With ROC analysis the cut-off point (maximizing the Youden index) was found to be 10 prescriptions, with a sensitivity of 0.602 and specificity of 0.794 as shown in figure 1.

Multivariate Analysis

Using the multiple regression model including age, sex, vital status, nicotine and alcohol histories, the first laboratory test results after admission and the number of drug prescriptions during hospital stay showed that only five parameters reached statistical significance. In the study population, an increase in temperature, decreased erythrocytes, low thrombocytes and increased number of drugs were independent predictors for the occurrence of an ADR. Alcohol consumption decreased the likelihood for ADRs (table II).

In a further multiple analysis model, excluding alcohol from consideration due to the high rate of missing data (26%), female sex (besides the other four predictors mentioned above) reached significance for an increased risk of ADRs. Body temperature, erythrocytes, thrombocytes and number of drugs remained independent in this model (table III).

We also assessed the difference in prediction accuracy of models including and excluding laboratory tests. Excluding the laboratory parameters reduced the area under the plasma concentration-time

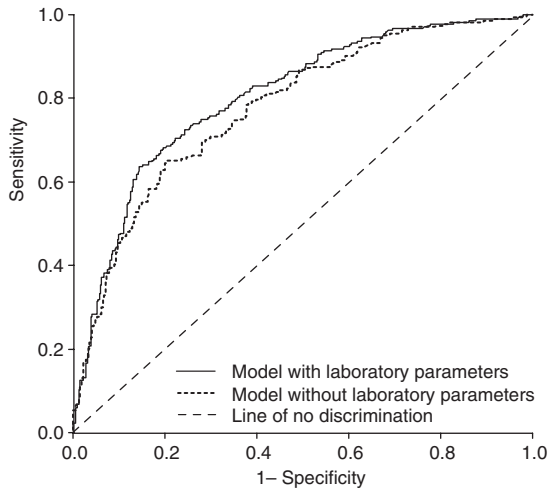

Fig. 1. Receiver Operating Characteristic model: adverse drug reaction predictability with and without laboratory test results.

Table III. Results of the multivariate analysis of significant influencing factors for the occurrence of an adverse drug reaction, excluding alcohol consumption. Estimates are additionally adjusted for age, heart rate, hospital stay, department effect and laboratory

Predictors	Odds ratio (95% CI)	p-Value
Sex	1.562 (1.001, 2.438)	0.0495
Body temperature	1.659 (1.172, 2.348)	0.0043
Erythrocyte count	0.445 (0.230, 0.863)	0.0166
Thrombocyte count	0.773 (0.617, 0.967)	0.0243
No. of drugs	1.120 (1.079, 1.162)	<0.0001

curve (AUC) slightly (AUC 0.80 vs 0.78; p = 0.0023) as shown in figure 1. Using the best cut-off point (maximal Youden index) to divide between ADR-positive and -negative patients, both models reached only moderate sensitivities (0.64 and 0.65, with specificities of 0.86 and 0.80, respectively).

Discussion

The practice of medicine depends on the science of prediction. Prediction depends on clinical observations or on laboratory variables or factors that are linked to outcome. Physicians often have a lack awareness of ADRs in hospitalized patients.[28,51-55] One of the reasons may be that it is difficult to identify patients at risk of ADRs in clinical practice. To help improve this, predictability and preventability could be evaluated retrospectively by scores described in the literature and as shown in the current study.[49,56] Nevertheless, predictive factors for ADRs in individuals are needed. The aim of this study was to characterize risk factors associated with ADRs during hospital admission, in order to focus physicians' awareness on these patients at the first physician-patient contact.

In the current study of hospital admissions, increased temperature, low thrombocyte levels, low erythrocyte levels, multiple drug use and female sex were established as independent predictors of ADRs. Previous studies have examined many potential risk factors associated with ADRs in a variety of settings.[5-7,9,10,13,16,17,33,57,58] These studies differ in their methods of identifying ADRs, their inclusion criteria for adverse drug events (ADEs) or ADRs, their evaluation scores, the statistical methods used and the variables examined. However, only few multicentre studies have used the 'gold standard of pharmacovigilance' – intensive prospective ADR detection – and studies in the field of pharmacovigilance using multiple regression models encompassing the data mentioned above are rare. In such studies, the broad range of ADR incidence varied from 0.01% up to 69%.[3,5,9,42] In the current study, where prospective intensive pharmacovigilance was used, the ADR rate was 38%. Other prospective pharmacovigilance studies using intensive surveillance methods for ADRs have been consistent with this result.[6,12]

Gurwitz and Avorn[58] concluded that interpretation of the results of studies incorporating the above methods is often limited by inconsistent definitions, different statistical methods, and failure to control for important age-related covariates including the clinical status of the patient and the number of medications that a patient is receiving.

In our model we have incorporated a very limited number of potential predictive factors for ADRs. Therefore, additional models need to be explored that incorporate more variables (e.g. co-morbidity scores) to obtain different perspectives on potential risk profiles. However, to improve the statistical power of ADR prediction it is necessary to use a much larger study population, which can only be generated by an international network, e.g. using clinical data warehouse technology.[59] One difficulty in this process is that there are multiple categories of potential predictors. These categories need to be broken down into several defined, structured and standardized factors by an international expert panel. Web-based data capture on these standardized factors could then enable international collaboration on this important issue in drug safety. In this regard, our results may provide a foundation for and influence the future design and implementation of such models.

Increasing age or the presence of signs of organ function impairment, such as renal or hepatic insufficiency, are often cited as one of the potential risk factors of ADRs in univariate analyses.[3,5,7,8,15,16,19,20,30,31,60,61] We could not confirm this finding in our multiple regression model, de-

spite significant correlations of several variables in univariate analysis. This is in line with other studies using multiple analysis or logistic regression models based on data attained by intensive pharmacovigilance methods.[3,5,6,8,12,14]

Malnutrition was also correlated with the presence of ADRs or ADEs in literature reports.[3,32] However, in our population, neither albumin nor BMI were independent ADR predictors. In our population, only raised temperature, female sex, decreased thrombocytes, multiple number of drugs and anaemia predicted ADRs. The presence of low thrombocytes was also identified as an ADR predictor in two studies.[1,32] For anaemia, González-Martín et al.[13] revealed a tendency towards lower haematocrit levels in patients with ADRs.

On the other hand, there is consensus about the predictive power of large numbers of prescribed drugs in individual patients as an independent predictor of ADRs.[3,7,13,15,29] Using a ROC model we could establish a critical cut-off point of more than ten drug prescriptions during hospital stay that predicts ADRs. This finding also confirmed the result of Camargo et al.[6] Using a multiple logistic regression model, Carbonin et al.[7] found that taking more than four drugs simultaneously on medical wards positively correlated with ADR occurrence (OR 2.94).

Sex as a risk factor for ADRs remains a matter of debate.[3-7,10,25] There are several factors that might explain why sex could be a risk factor for ADRs, e.g. differences in circulating hormone levels and use of medications that might alter drug metabolism in the liver.[17] In the current investigation, sex showed no significant influence on the occurrence of ADRs when alcohol consumption was included in the statistical model. When alcohol consumption was excluded from the model, female sex reached weak significance as a predisposing factor of ADRs. This finding is hard to interpret. If alcohol consumption prevents ADRs, perhaps by enzymatic induction, or stimulation of the microsomal ethanol oxidizing system, this should be the main target for further investigations.

It should be borne in mind that because of the high rate of missing data on alcohol consumption (26%), the analyses were conducted in only a subpopulation. Furthermore, weak anamnestic data on alcohol consumption may bias this result. In contrast to our results, retrospective analyses in elderly medical patients by Onder et al.[22,23] concluded that moderate alcohol intake is associated with an increase in ADRs and that this effect seemed more evident among women than in men. In the multiple logistic regression, Carbonin et al.[7] positively correlated drinking alcohol with ADR occurrence in hospitalized patients in internal and geriatric wards. The multiple analysis by Caamaño et al.[5] showed that none of sociodemographic and health habit variables considered were associated with a higher incidence of ADRs at hospital admission. With regard to tobacco use, previous analyses reveal consensus that there is no evidence for an impact on ADRs. This finding is in line with our results.

Despite using a multiple regression model, a definite discrimination between causative or confounding factors in predicting an ADR is not possible. Our model is limited by the number of factors included in the analysis and the sample size. Furthermore, using the best cut-off point to divide between ADR-positive and -negative patients, both models reach only moderate sensitivities. This indicates that although the variables are predicting factors, their predictive ability is limited even in combination, and other (unknown) factors still need to be investigated.

Conclusion

In our study population the multiple regression model based on age and sex, vital signs at admission, nicotine and alcohol consumption, first laboratory test results and drug prescriptions after admission indicated that only raised temperature, decreased thrombocytes and erythrocytes, multiple drug use and female sex were independent predictors for ADRs. Taking these results into account, physicians will be able to focus early on patients at risk for ADRs. To minimize ADR occur-

rence, ADR predictors should be implemented into the clinical pathway.

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