

W. Mühlberg
K. Becher
H.-J. Heppner
S. Wicklein
C. Sieber

Acute poisoning in old and very old patients: a longitudinal retrospective study of 5883 patients in a toxicological intensive care unit

Akute Vergiftungen (sehr) alter Patienten: Longitudinale retrospek- tive Analyse bei 5883 Patienten einer toxikologischen Intensivstation

■ **Summary** Although morbidity and mortality of acute poisoning are increased in elderly compared to younger patients, little has been published on this topics in the last years (Medline search). To investigate the influence of age on the clinical course of acute poisoning with different toxic agents, a longitudinal retrospective study at the Toxicological In-

tensive Care Unit (ICU) of the 2nd Department of Internal Medicine (Klinikum Nürnberg, Germany) was performed.

A total of 5883 patients treated at our toxicological ICU were enrolled into the study, including all patients of the years 1982, 1992, and 1997. These three years were selected to investigate possible time-dependent changes of intoxication characteristics and quality of therapy at our ICU over a time span of 15 years.

For each patient the following data were obtained from a standardized toxicological record: age, gender, toxic agents responsible for acute poisoning, and length of stay at the toxicological ICU. For a subgroup of 3740 patients, the cause of acute poisoning and the clinical outcome was also recorded.

As compared with younger patients, mean length of stay at the ICU, indicating a more serious course of acute poisoning, was prolonged in elderly and, i.e., in very old patients ($p < 0.001$). However, this prolongation of time at the ICU was only observed in elderly patients poisoned with drugs or with mixed poisoning including drugs, while mean length of stay was *not* prolonged in elderly patients poisoned with alcohol, with illegal drugs, chemicals, animal/plant poison, or other toxic agents.

Patients with the highest risk of dying in the ICU after acute poisoning were elderly patients attempting suicide with drugs. Mortality in 3740 patients with acute poisoning was 0.24%, while it was 2.17% in the 184 patients being 65 years old or older. Thus, mortality was 9-fold higher in the elderly.

Mean length of stay at the ICU decreased significantly from 1982 to 1992 and to 1997 ($p < 0.001$) indicating an improvement of the therapeutical ICU management of acute poisoning and/or less dangerous toxic agents (i.e. less barbiturates). The age-dependent increase of the length of stay at the ICU until very old age (> 80 years) was most pronounced in 1982 and also declined markedly until 1997.

Age, suicide attempt, and ingestion of (multiple) drugs seem to be risk factors for a higher mortality and a prolonged stay in the ICU after acute poisoning. Although in general the clinical course after poisoning has more complications and an impaired prognosis in old age, each category of toxic agents (drugs, alcohol, chemicals, etc.) has its own special “risk profile” for elderly patients. However, due to advances in modern ICU medicine the general prognosis of acute poisoning is good in old and even in oldest old patients.

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Priv.-Doz. Dr. Wolfgang Mühlberg (✉)
Dr. Klaus Becher · Dr. Hans-Jürgen Heppner
Susanne Wicklein · Prof. Dr. Cornel Sieber
Chair of Internal Medicine and Gerontology
Institute for Biomedicine of Aging
University of Erlangen-Nürnberg and
Toxicological Intensive Care Unit
and Poison Information Center of the
2nd Department of Internal Medicine
Klinikum Nürnberg
Heimerichstr. 58
90419 Nürnberg, Germany
Tel.: 09 11 / 3 98 56 48
Fax: 09 11 / 3 98 56 49
E-Mail:
muehlberg@klinikum-nuernberg.de

■ **Key words** Age – acute poisoning – clinical course – intensive care unit – mortality – drugs

■ **Zusammenfassung** Obwohl akute Vergiftungen im Alter eine erhöhte Morbidität und Mortalität aufweisen, findet man nur wenig Literatur zu dieser Thematik (MEDLINE-Recherche 1980–2005). Dies gilt besonders für hochbetagte Patienten (≥ 80 Jahre). Ziel der vorliegenden retrospektiven Langzeitstudie war die Untersuchung der Frage, ob sich die Häufigkeit und der Verlauf akuter Vergiftungen bei älteren und hochbetagten Patienten von der jüngerer Patienten unterscheiden.

5883 Patienten (davon 351 ≥ 65 Jahre), die wegen einer akuten Vergiftung in den Jahren 1982, 1992 und 1997 auf unserer toxikologischen Intensivstation (Med. Klinik 2, Klinikum Nürnberg; Lehrstuhl Innere Medizin-Gerontologie der Universität Erlangen-Nürnberg) lagen, wurden in die Studie aufgenommen. Die Jahre 1982, 1992 und 1997 wurden ausgewählt, um über einen Zeitraum von 15 Jahren mögliche zeitabhängige Veränderungen der Häufigkeit und des Verlaufs akuter Vergiftungen und vor allem auch der „Therapieeffizienz“ unserer toxikologischen Intensivstation zu untersuchen. Mit einem standardisierten Fragebogen wurden für jeden Patienten Alter, Geschlecht, Name und Substanzklasse des Giftes sowie die Verweildauer auf

der toxikologischen Intensivstation erfasst. Für eine Untergruppe von 3740 Patienten wurden zudem noch der Grund für die akute Vergiftung (Suizidversuch, akzidentelle Überdosierung, akzidentelle Vergiftung zuhause, am Arbeitsplatz, Allergie, unbekannte Ursache) und der genauere klinische Verlauf (reguläre Entlassung, Weiterverlegung, Exitus letalis, irreguläre Entlassung etc.) ermittelt.

Die Verweildauer auf der toxikologischen Intensivstation, ein „Marker“ für die Schwere und die Komplikationsrate des klinischen Verlaufs einer akuten Vergiftung, war im Mittel bei den älteren und besonders bei den hochbetagten Patienten deutlich ($p < 0,001$) verlängert (im Vergleich zu jüngeren Patienten). Diese altersabhängige Zunahme der Verweildauer wurde jedoch *nur* bei Vergiftungen mit Pharmaka und bei Mischintoxikationen (mit mindestens einem Pharmakon) beobachtet, *nicht* jedoch bei Vergiftungen mit Alkohol, Drogen, Chemikalien, pflanzlichen/tierischen Giften oder anderen Giftstoffen.

Die Patienten mit dem höchsten Letalitätsrisiko durch eine akute Vergiftung waren ältere Patienten, die mit Arzneimitteln Suizid versucht hatten. Die Gesamt-Letalität der 3740 Vergiftungspatienten betrug 0,24%, bei den Patienten ≥ 65 Jahren dagegen 2,17%! Die Letalität nach Vergiftungen bei älteren Patienten war also im Vergleich zur Gesamt-Letalität bei Vergiftungen um das 9fache erhöht!

Die mittlere Verweildauer auf der toxikologischen Intensivstation nahm von 1982 über 1992 bis 1997 signifikant ab ($p < 0,001$), was durch die zwischenzeitlichen Verbesserungen der intensivmedizinischen Therapie akuter Vergiftungen und/oder durch die abnehmende Verwendung besonders gefährlicher Giftstoffe (vor allem Barbiturate) erklärt werden kann. Die noch 1982 nachweisbare deutlich verlängerte intensivmedizinische Verweildauer besonders bei hochbetagten Patienten, der ausgeprägte Unterschied zwischen jungen und sehr alten Patienten, war 1997 kaum mehr nachweisbar.

Hohes Alter, Suizidversuch und Medikamente als Vergiftungsursache (allein oder als Mischintoxikation) sind die Hauptrisikofaktoren für eine erhöhte Komplikationsrate (mit verlängerter intensivmedizinischer Verweildauer) bei akuten Vergiftungen. Generell wird mit zunehmendem Alter die Prognose von Intoxikationen schlechter, doch hat offenbar jede Substanzklasse von Giften (Medikamente, Drogen, Alkohol, Chemikalien u. a.) ihr eigenes spezielles Risikoprofil beim älteren Patienten.

Aufgrund der Fortschritte der toxikologischen Intensivmedizin ist die Prognose akuter Vergiftungen bei älteren und auch bei hochbetagten Patienten trotzdem gut.

■ **Schlüsselwörter** Alter – Akute Vergiftungen – Intensivmedizin – Pharmaka – Letalität

Introduction

About 40% of poisonings after drug administration occur in the elderly. These poisonings include suicide attempts, unintentional acute overdoses or chronic therapeutic intoxications, and adverse drug reactions [5, 12–16]. A marked proportion of the disease conditions in elderly patients is related to adverse reactions to prescribed drugs [13]. Age per

se is not an independent risk factor for adverse drug reactions (ADR), but age-dependent factors such as polymedication, multiple diseases and changes in pharmacokinetics and pharmacodynamics seem to be responsible for the risk of developing ADR [5]. Therefore, age and its implications may also influence the clinical course of acute poisoning in patients.

Poisoning is a significant problem in the elderly. The majority of poisonings in older people are unintentional and may result from dementia and confusion, improper use of the product, improper storage or mistaken identities [12]. Depression is also common in the elderly and suicide attempts are more likely to be successful in this age group [16]. Although morbidity and mortality of poisoning are higher in the elderly than in younger patients [14], little has been published on this topic (Medline search from 1990 to 2005). Thus we undertook a longitudinal retrospective study in the medical Intensive Care Unit (ICU) of our Toxicology Center to investigate the influence of age (including very old age, ≥ 80 years) on the clinical course of acute poisoning with different toxic agents.

We also investigated (over a time span of 15 years) possible time-dependent changes of intoxication characteristics and of effectiveness of the ICU therapy.

Materials and methods

■ Study design and patients

The following data were obtained from a standardized toxicological report of 5883 patients: age, gender, month and year of admission, toxic agent(s) responsible for acute poisoning (alcohol, drugs, illegal drugs, chemicals, animal and plant poisons, mixed poisoning including drugs, other toxic agents), and length of stay at the toxicological ICU. For a subgroup of 3740 patients, the cause of acute poisoning (unknown reason, suicide attempt, accidental overdosing, accident at home, accident at work, allergy), and the clinical outcome (regular discharge, admission to another hospital department, death, and irregular discharge which means the patient left the ICU without permission) was recorded.

In addition, category and name of drugs (cardiovascular drugs, analgesics and anti-inflammatory drugs, oral hypoglycemics, psychoactive drugs, i.e., tranquilizer and benzodiazepines, neuroleptic drugs and cyclic antidepressants) and of chemicals were recorded.

Seriousness of clinical course of the acute poisoning was estimated by two variables: a) length of stay at the toxicological ICU (days) and b) clinical outcome.

A total of 5883 patients admitted to the ICU of our toxicology center with the diagnosis of acute poisoning of the years 1982, 1992, and 1997 were enrolled to the study. These three years were selected to investigate possible time-dependent changes of intoxication characteristics and quality of therapy at our ICU over a time span of 15 years.

The diagnosis "acute poisoning" includes acute intoxications and symptomatic poisoning due to chronic intoxication. The patients admitted to our toxicology center came from the city of Nuremberg and from the region of northern Bavaria/Germany. Only patients 16 years old or older are admitted to our center; children are excluded.

To investigate the influence of age patients were divided in two groups: those who were 65 years old or older, and those younger than 65 years. To analyze the influence of very old age and for a more subtle analysis, patients were also divided in the four age groups < 60 , 60–69, 70–79, and ≥ 80 years.

■ Statistics

The statistics program SPSS for Windows 12.0 was used for all statistical evaluations. Differences between elderly and younger patients were tested using the non-parametric 2-tailed Mann-Whitney test (U-test) or the Kruskal-Wallis test, if appropriate. Important results are demonstrated graphically as means with 95% confidence intervals (CI) or as box-plots (box and whiskers plot: median values, 25% and 75% percentile (box), minimum and maximum values ("whiskers"), and extreme values (*). Values with a distance from the 75% or 25% percentile between 1.5 and 3 box lengths are marked with open circles (O). The level of statistical significance was set at $p < 0.05$ (2-tailed-test). N is the number of patients of each group.

Results

A total of 351 patients, representing 5.9% of the 5991 patients with acute poisoning, were 65 years old or older (age range from 65 to 97 years, mean age 75.0 ± 7.3 years). The age range of the "younger" group was 8 to 64 years, mean age 34.5 ± 12.3 years.

In young, old, and very old patients with acute poisoning, marked differences of the length of stay at the toxicological ICU were observed (Fig. 1). This difference between age groups is statistically significant ($p < 0.001$, Kruskal-Wallis test) and increases with age.

In the subgroup of 3740 patients, mean length of stay in the toxicological ICU also varied widely between elderly (≥ 65 years) and younger (< 65) patients (old vs young: 3.2 ± 5.6 days vs 1.0 ± 1.6 days, $p < 0.001$).

Dividing all patients ($n = 5883$) into different groups related to the toxic agents ingested, a more differentiated result occurs (Fig. 2): an age-dependent difference of the mean length of stay was *only* seen

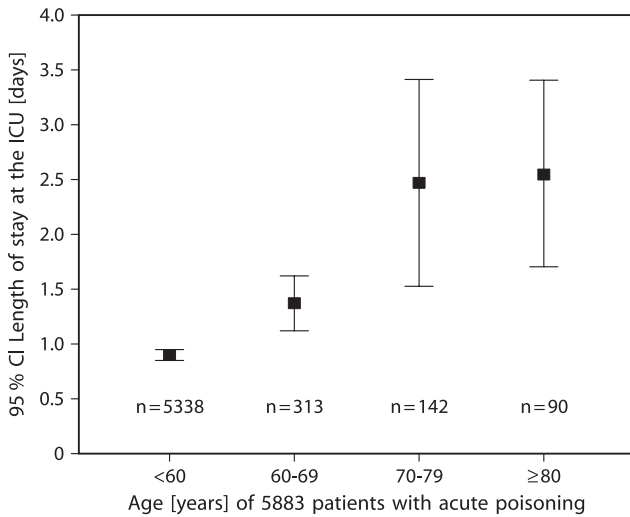


Fig. 1 Length of stay in the Toxicological Intensive Care Unit (ICU) after acute poisoning in young, old, and very old patients. The difference between age groups is statistically significant ($p < 0.001$, Kruskal-Wallis test) and increases with age

in the patients with acute poisoning with drugs (old vs young: 3.6 ± 5.0 days vs 1.3 ± 2.1 days, $p < 0.001$) and in the patients with mixed poisoning (old vs young: 2.3 ± 2.2 days vs 0.8 ± 1.1 days, $p < 0.001$). No age-dependent difference was seen in the patients intoxicated with alcohol, with illegal drugs, with chemicals, with animal/plant poisons or with other toxic agents. It should be noted that all patients with mixed poisoning had at least ingested one drug too.

Relating the length of stay in the ICU to the cause of the acute poisoning, age-dependent differences of the mean length of stay could be shown again (Fig. 3): in the patients with unknown reason (old vs young: 3.5 ± 5.5 days vs 1.0 ± 1.6 days, $p < 0.05$), in the patients with suicide attempt (old vs young: 4.7 ± 6.1 days vs 1.7 ± 2.2 days, $p < 0.001$), and in patients with accidental overdose (old vs young: 2.3 ± 5.8 days vs 0.6 ± 1.0 days, $p < 0.001$). In patients with acute poisoning caused by accident at home, by accident at work or by an allergy, no age-dependent differences in the length of stay were seen (Fig. 3). Thus, elderly patients with suicide attempt had to stay in the ICU for the longest time (4.7 days), as compared with all other groups of patients.

The outcome of the patients – again related to the length of stay in the ICU – for the two age groups is shown in Figure 4. Mean length of stay in the ICU was prolonged in the elderly patients with regular discharge (4.12% of all patients with regular discharge were elderly patients; old vs young: 2.7 ± 4.8 days vs. 1.0 ± 1.6 days, $p < 0.001$) and in the elderly patients with transfer to another department (10.85% of all patients with transfer to another department were elderly; old vs young: 4.0 ± 4.3 days vs 1.5 ± 2.3 days, $p < 0.001$).

Patients with transfer to another hospital department, indicating a more complicated course of acute poisoning, showed a higher percentage of elderly (10.85%) than patients with regular discharge (4.12%).

The highest relative rate of elderly patients was found in those patients who died after acute poison-

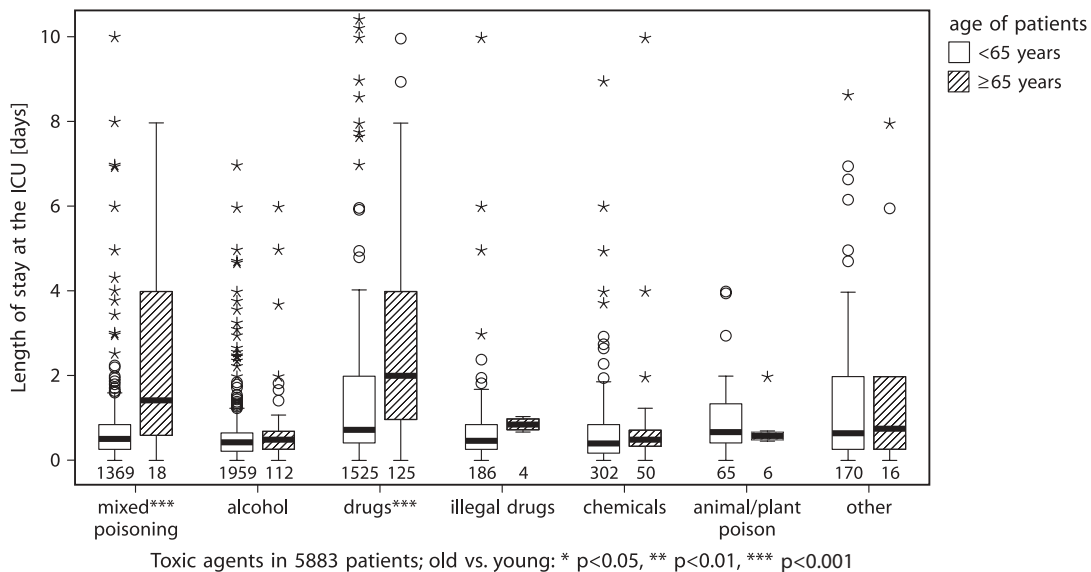


Fig. 2 Length of stay at the Toxicological Intensive Care Unit (ICU) after acute poisoning in elderly and younger patients in relation to the toxic agents. Statistically significant differences ($p < 0.001$, 2-tailed U-test) between

young and old patients occur only in the groups poisoned with drugs or with mixed poisoning. For all other toxic agents, no age-dependent differences were observed

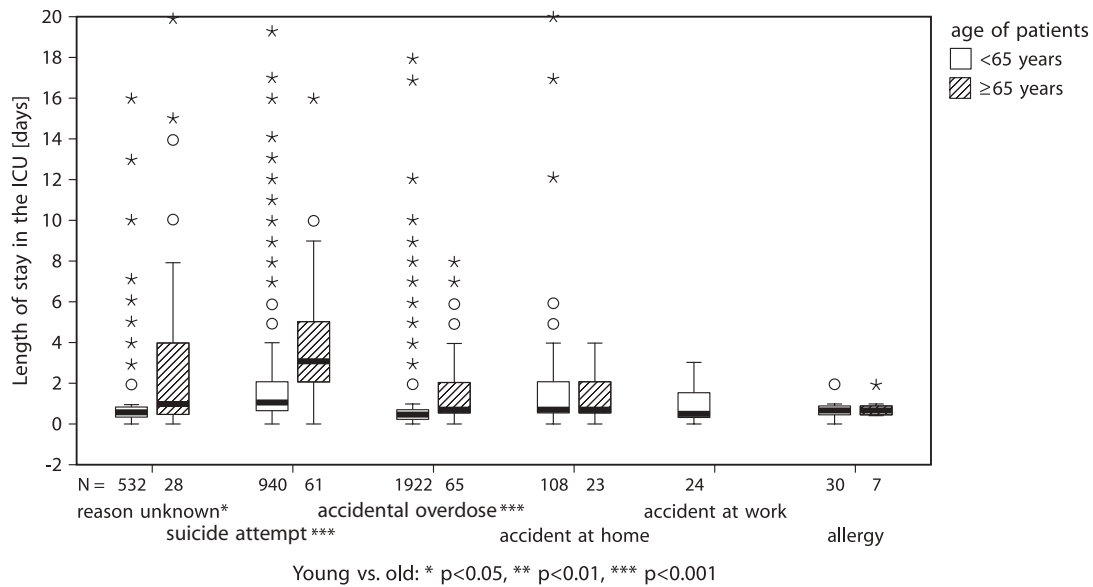


Fig. 3 Length of stay in the ICU after acute poisoning in elderly and younger patients in relation to the cause of poisoning (n=3740 patients)

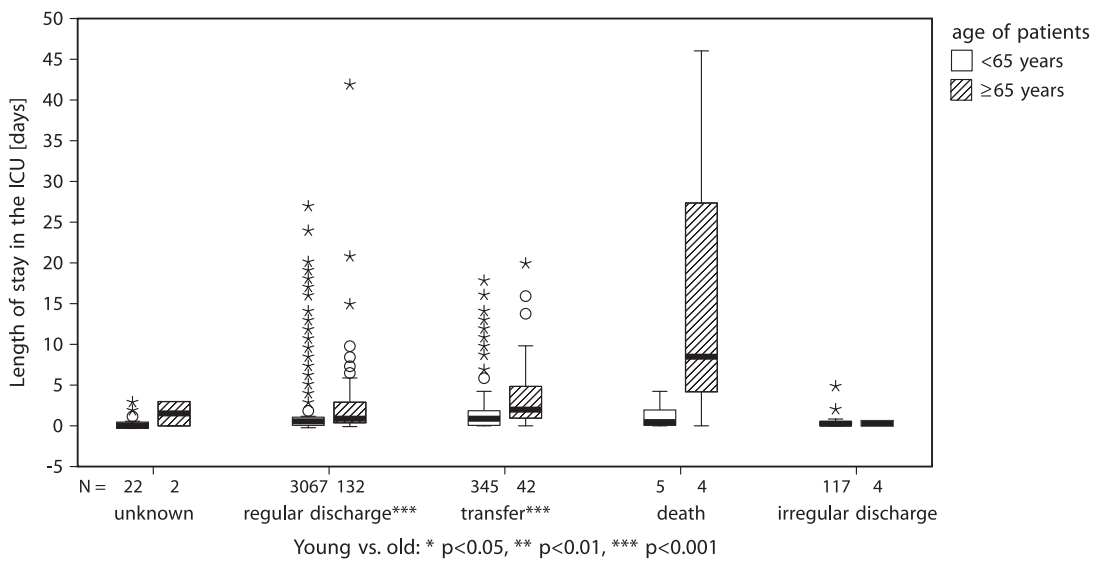


Fig. 4 Length of stay at the ICU after acute poisoning in elderly and younger patients in relation to the clinical outcome (n=3740 patients)

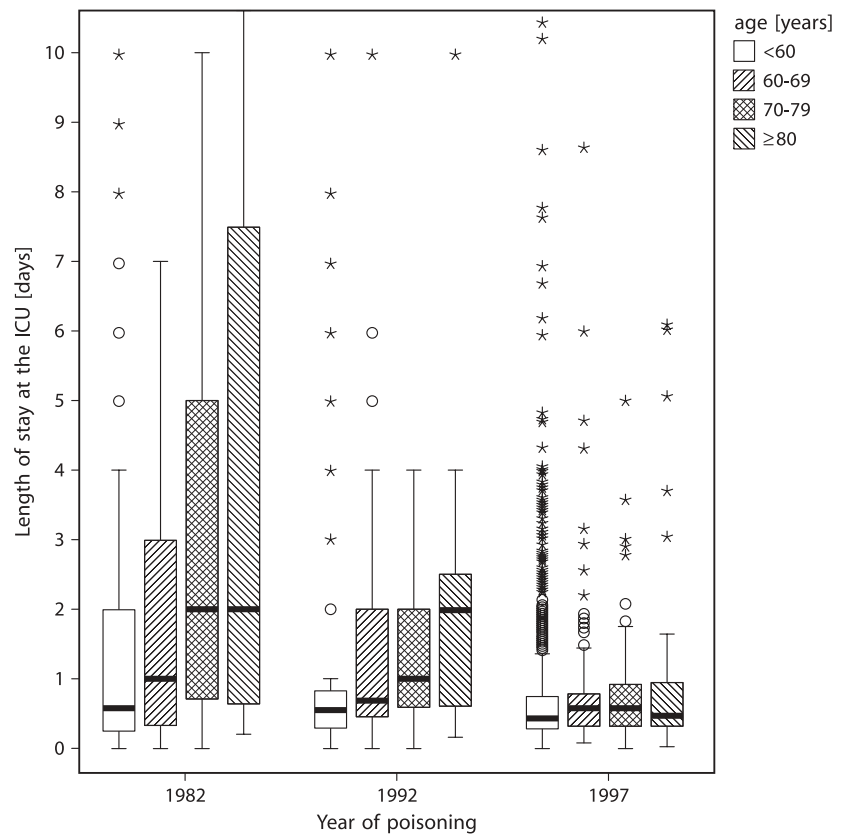
Table 1 Acute poisoning with lethal outcome (9 of 3740 patients)

■	87 years, male, suicide, drug overdose (barbiturate)
■	75 years, male, suicide, drug overdose (drugs unknown)
■	74 years, male, suicide, drug overdose (barbiturate)
■	70 years, male, accidental alcohol intoxication
■	61 years, female, suicide, drug overdose (digoxin, lormetazepam)
■	55 years, male, suicide, chemicals (organophosphate)
■	40 years, male, suicide, drug overdose (drugs unknown)
■	27 years, male, suicide, chemicals (organophosphate)
■	16 years, female, suicide, drug overdose (acebutolol, penbutolol, oxazepam, metoclopramide)

ing (Fig. 4 and Table 1): four of the nine patients who died were 65 years and older. If the cut-off point of being “an elderly patient” was set to 55 years (11.1% of all patients), even two-thirds of the patients who died were elderly (Table 1).

Mean length of stay in the ICU decreased significantly from 1982 to 1992 to 1997 ($p < 0.001$, Kruskal-Wallis test, see Fig. 5). The age-dependent increase of the length of stay in the ICU until very old age (>80 years) was most pronounced in 1982 and declined markedly until 1997.

Fig. 5 Mean length of stay at the ICU decreased significantly from 1982 to 1992 to 1997 ($p < 0.001$, Kruskal-Wallis test). The age-dependent increase of the length of stay in the ICU until very old age (>80 years) was most pronounced in 1982, declining markedly until 1997



Discussion

Pichot et al. [14] found in 92 elderly patients (>70 years) with suicidal acute drug poisoning a mortality of 14% while mortality was only 1% in all 2762 patients of their study. Over all mortality in the subgroup of 3740 patients in our study was 0.24%, while it was 2.17% in our 184 elderly patients. Thus, mortality in the elderly patients was 9-fold higher as compared with the mortality of all our patients with acute poisoning. In good accordance with the results of Pichot et al. [14], we observed the longest mean length of stay in the ICU in elderly patients with suicidal poisoning. Chodorowski and Anand [6] investigated 98 patients with suicidal tricyclic antidepressants poisoning; their mean age was 35 years. Only five patients died but three of them were aged.

Although elderly patients (>65 years) represent only a small percentage of the patients with acute poisoning, the morbidity and mortality in these elderly is much higher. The prolonged stay in the ICU after acute poisoning in the elderly patients of our study, indicating a more serious clinical course, again underlines this finding. This is not a surprising result. There are several possible explanations:

- Acute poisoning and stay in an ICU is frequently associated with mechanical ventilation. Advanced age is an important prognostic factor for the development of acute respiratory failure in ICU patients [10, 18].
- Age-dependent factors such as multiple diseases and polymedication, improper use of the drug, improper storage or mistaken identities – which may result from dementia and confusion in the elderly patients – may lead to an increased frequency of mixed poisonings (most of them unintentional) in the elderly patients [2, 11]. The most frequent cause of acute poisoning in the elderly patients of our study was accidental overdosing of drugs (65 patients), followed by suicide attempts (61 patients). It is well known that the rate of complications is greatest in the patients with mixed poisonings [17].
- Age-dependent changes in pharmacokinetics and pharmacodynamics seem to be responsible for the increased risk of elderly patients of developing adverse drug effects [1, 5, 13]. The same conditions may be the reason for the prolonged course of acute poisoning and the higher mortality rate observed in the elderly patients of our study.

There is a close relationship between the rate of adverse drug reactions and renal function. Declining renal function, a reduction in both renal blood flow and glomerular filtration rate, is a major contributor to drug toxicity in the elderly. This age-dependent decline of the renal elimination of drugs may also be important for the clinical course of acute poisoning in the elderly.

An interesting aspect of our study seems to be the observation that an age-dependent prolongation of the mean length of stay in the ICU – indicating a more complicated course of acute poisoning – and a higher mortality was primarily seen in patients poisoned with drugs: drugs or mixed poisoning with drugs as toxic agents (Fig. 2 and Table 1). Most drugs, including metabolites, are excreted via the kidneys: biliary excretion and elimination via the feces play only a minor role. Therefore, the age-dependent decline of renal function may also play a key role for the prolonged and more serious course of acute poisoning in the elderly.

It should be noted in this context that there was no increase in the mean length of stay in the ICU in elderly patients poisoned with alcohol, illegal drugs, chemicals, animals/plants, and other toxic agents (see Fig. 2). Alcohol is eliminated only by hepatic metabolism: in contrast to the renal function, the hepatic elimination capacity is not or only to a lesser degree declining with age [15].

Although studies confirm the vulnerability of elderly people to the destructive effects of alcohol [3, 7–9], Friedman et al. [8] found no effect of alcohol problem drinking on physical health status of elderly patients seen in an emergency department. Brodov et al. [4] also found no age-dependent differences in patients with food poisoning.

There are some positive aspects of our study. Mean length of stay at the ICU decreased significantly from 1982 to 1992 and to 1997 ($p < 0.001$) indicating an improvement of the therapeutical ICU management of acute poisoning and/or less dangerous toxic agents (i.e. less barbiturates) (Fig. 5). The age-dependent increase of the length of stay in the

ICU until very old age (>80 years) was most pronounced in 1982 and declined markedly until 1997.

Conclusions

As compared with younger patients, mean length of stay at the ICU, indicating a more serious course of acute poisoning, was prolonged in elderly and especially in very old patients. However, mean length of stay in the ICU was prolonged *only* in elderly patients poisoned with drugs or with mixed poisoning including drugs, while mean length of stay at the ICU was *not* prolonged in elderly patients poisoned with alcohol, with illegal drugs, with chemicals, with animal/plant poisons or with other toxic agents.

ICU patients with the highest risk of dying after acute poisoning were elderly patients committing suicide attempts with drugs.

Age-dependent risk factors responsible for adverse drug reactions in the elderly such as multiple diseases, poly medication, and changes in pharmacodynamics and pharmacokinetics (i.e., the age-dependent decline of renal function) seem to be responsible for the more serious clinical course of acute poisoning in elderly patients, too.

A positive aspect of our study was the observation that mean length of stay in the ICU decreased significantly from 1982 to 1992 and to 1997 ($p < 0.001$) indicating an advance of the therapeutical ICU management of acute poisoning and/or the use of less dangerous toxic agents (i.e. less barbiturates). The age-dependent increase of the length of stay at the ICU until very old age (>80 years) was most pronounced in 1982 and declined markedly until 1997.

Therefore, due to advances in modern ICU medicine, the general prognosis of acute poisoning is good in old and even in very old patients. It is fully justified to admit even a very old patient (>80 years) with an acute poisoning to an ICU.

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