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Clinical Study

In-hospital mortality after pre-treatment with antiplatelet agents or oral anticoagulants and hematoma evacuation of intracerebral hematomas



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ABSTRACT

Pre-treatment with antiplatelet agents is described to be a risk factor for mortality after spontaneous intracerebral hemorrhage (ICH). However, the impact of antithrombotic agents on mortality in patients who undergo hematoma evacuation compared to conservatively treated patients with ICH remains controversial. This analysis is based on a prospective registry for quality assurance in stroke care in the State of Hesse, Germany. Patients' data were collected between January 2008 and December 2012. Only patients with the diagnosis of spontaneous ICH were included (International Classification of Diseases 10th Revision codes I61.0–I61.9). Predictors of in-hospital mortality were determined by univariate analysis. Predictors with P < 0.1 were included in a binary logistic regression model. The binary logistic regression model was adjusted for age, initial Glasgow Coma Score (GCS), the presence of intraventricular hemorrhage (IVH), and pre-ICH disability prior to ictus. In 8,421 patients with spontaneous ICH, pre-treatment with oral anticoagulants or antiplatelet agents was documented in 16.3% and 25.1%, respectively. Overall in-hospital mortality was 23.2%. In-hospital mortality was decreased in operatively treated patients compared to conservatively treated patients (11.6% versus 24.0%; P < 0.001). Patients with antiplatelet pre-treatment had a significantly higher risk of death during the hospital stay after hematoma evacuation (odds ratio [OR]: 2.5; 95% confidence interval [CI]: 1.24-4.97; P=0.010) compared to patients without antiplatelet pre-treatment treatment (OR: 0.9; 95% CI: 0.79-1.09; P = 0.376). In conclusion a higher rate of in-hospital mortality after pre-treatment with antiplatelet agents in combination with hematoma evacuation after spontaneous ICH was observed in the presented cohort.

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1. Introduction

Spontaneous hematomas are the most common type of intracerebral hemorrhage (ICH) [1]. Case fatality at 1 month ranges from 13.1% to 61% [2]. Oral anticoagulants are associated with increased mortality rates after ICH [3,4]. Some authors have found an increased mortality rate after pre-treatment with antiplatelet agents [5,6]. In a current systemic review pre-treatment with antiplatelet agents in ICH was associated with increased mortality, but not with functional outcome [7].

Currently, only 7.9% of patients in Germany and 6.9% of patients in the USA with spontaneous ICH have a hematoma evacuation performed [8,9]. For this reason, the number of operated ICH patients is very low in most published studies. However, the role of antiplatelet agents on mortality rate after hematoma evacuation in spontaneous ICH remains controversial. The combination of prior antiplatelet treatment and hematoma evacuation has also not been sufficiently assessed.

This study investigated the hypothesis that patients on antiplatelet agents with hematoma evacuation have a higher in-hospital mortality rate compared to patients managed with conservative treatment.

2. Methods

In this study, 8,421 patients with the diagnosis of spontaneous ICH were analysed (*International Classification of Diseases 10th Revision* codes I61.0–I61.9). The data used were obtained from a state-wide prospective stroke registry in the State of Hesse, Germany between January 2008 and December 2012. Patients' data were registered anonymously; therefore no Ethical Board



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approval was necessary. Outcome was determined with the modified Rankin Scale (mRS). Pre-ICH disability was defined as mRS >2 prior to ictus. Data were analysed using the Student's t-test or the Mann–Whitney U test for the comparison of continuous variables and the chi-square test for the comparison of categorical variables. A binary logistic regression model was used to observe the association between pre-treatment with antiplatelet agents or anticoagulants and in-hospital mortality. The binary logistic regression model was adjusted for age, initial Glasgow Coma Scale score (GCS), the presence of intraventricular hemorrhage (IVH), and pre-ICH disability. P < 0.05 was considered significant.

3. Results

Hematoma evacuation was documented in 595 patients (7.1%). Conservative treatment was reported in 7,826 patients (92.9%). The baseline characteristics of the cohort are shown in Table 1.

Patients on antiplatelet therapy were significantly older than patients without antiplatelet therapy (mean ± standard deviation 77.2 ± 10.0 years *versus* 70.1 ± 14.1 years; P < 0.001). Patients using oral anticoagulants were significantly older compared to patients without oral anticoagulants (76.1 ± 9.6 years *versus* 71.0 ± 14.1 years; P < 0.001). In conservatively treated patients, the rate of antiplatelet agents was significantly higher compared to operatively treated patients (25.9% *versus* 14.3%; P < 0.001). No differences were observed for patients on oral anticoagulants, whether operatively or conservatively treated (16.6% *versus* 16.2%; P = 0.800).

The rate of patients with pre-ICH disability (mRS >2) was 16.2%. The pre-ICH disability rate was higher in conservatively treated patients compared to operatively treated patients (19.0% *versus* 10.1%; *P* < 0.001). Patients with pre-ICH disability were more often on antiplatelet medication than patients without pre-ICH disability (19.7% *versus* 14.0%; *P* < 0.001). No significant difference between patients with pre-hospital mRS >2 and mRS \leq 2 was observed for the pre-treatment with oral anticoagulants (18.4% *versus* 18.3%; *P* = 0.936).

Overall in-hospital mortality was 23.2%. In-hospital mortality was decreased in operatively treated patients compared to conservatively treated patients (11.6% *versus* 24.0%; *P* < 0.001). However, favourable functional outcome (mRS ≤ 2) in the operated group was lower than in the conservative group (14.0% *versus* 24.9%; *P* = 0.001). We found no significant statistical association between lobar (*P* = 0.066) or cerebellar (*P* = 0.575) hematomas and in-hospital mortality. A cumulative univariate analysis of all other hematoma locations showed a positive statistical correlation with in-hospital mortality (*P* = 0.044).

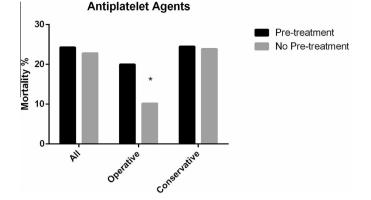


Fig. 1. Mortality rate of operatively treated patients with intracerebral hemorrhage on antiplatelet agents was twice that of patients without antiplatelet pre-treatment (20.0% *versus* 10.2). *P = 0.009.

In-hospital mortality was higher among patients on anticoagulants (30.8% *versus* not on anticoagulants 21.7%; P < 0.001), but not in patients on antiplatelet agents (24.3% *versus* not on antiplatelet agents 22.8%; P = 0.141).

In-hospital mortality rate was higher (20.0% *versus* 10.2; P = 0.009) in operatively treated patients on antiplatelet agents compared to patients without antiplatelet medication (Fig. 1). No differences were observed in the conservatively treated group (24.5% *versus* 23.9; P = 0.564).

In-hospital mortality rate was increased for conservatively treated patients on oral anticoagulants compared to patients without oral anticoagulants (32.3% versus 22.4%; P < 0.001) (Fig. 2). In the operatively treated group no differences in mortality rates for patients with or without oral anticoagulants were detected (11.1% versus 11.7%; P = 0.869).

The results of the binary logistic regression model are summarized in Table 2. Pre-treatment with oral anticoagulants (OR: 1.6; 95% CI: 1.42–1.83; P < 0.001) was confirmed as a predictor of in-hospital mortality in the regression analysis. However, after adjustment for age, pre-ICH disability, GCS, and IVH, pre-treatment with oral anticoagulants remained an independent predictor of in-hospital mortality, but only among conservatively treated patients (OR: 1.6; 95% CI: 1.35–1.94; P < 0.001).

Pre-treatment with antiplatelet agents was not a predictor of in-hospital mortality in the unadjusted overall analysis (OR: 1.1; 95% CI: 0.97-1.22: P = 0.141). However, after adjustment for age, pre-ICH disability, GCS, and IVH, pre-treatment with antiplatelet agents was confirmed as an independent predictor of in-hospital

Table 1

Basic characteristics and univariate analysis of 8,421 patients with intracerebral hematoma in the State of Hesse, Germany, between January 2008 and December 2012

	Overall (n = 8421)	Operative therapy (n = 595)	Conservative therapy (n = 7826)	P value
Mean age, years (± SD)	71.9 ± 13.6	63.3 ± 14.6	72.5 ± 13.3	<0.001
Female sex, n (%)	4042 (48.0)	273 (45.9)	3769 (48.2)	0.284
Pre-hospital mRS >2, n (%)	1550 (18.4)	60 (10.1)	1487 (19.0)	< 0.001
Median GCS at admission (P25–P75)	12 (7-15)	9 (3-13)	13 (7-15)	< 0.001
IVH, n (%)	1230 (14.6)	68 (11.4)	1162 (14.8)	0.023
Localisation, n (%)				
Lobar	2142 (25.4)	239 (40.2)	1903 (24.3)	< 0.001
Cerebellar	638 (7.6)	116 (19.5)	522 (6.7)	< 0.001
Other	5641 (67.0)	240 (40.3)	5401 (69.0)	< 0.001
Antiplatelet agents, n (%)	2113 (25.1)	85 (14.3)	2028 (25.9)	< 0.001
Oral anticoagulants, n (%)	1370 (16.3)	99 (16.6)	1271 (16.2)	0.800
In-hospital mortality, n (%)	1950 (23.2)	69 (11.6)	1881 (24.0)	< 0.001
Unfavourable outcome (mRS >2) at discharge, n (%)	5895 (70.0)	503 (84.5)	5376 (68.7)	< 0.001

GCS = Glasgow Coma Scale, IVH = intraventricular haemorrhage, mRS = modified Rankin Scale, P = percentile, SD = standard deviation.

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