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Prognostic significance of age in patients with acute ischaemic stroke treated with intravenous thrombolysis

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ABSTRACT

Aim of the study. To assess the influence of age on long-term functional outcome in patients with acute ischaemic stroke (AIS) treated with intravenous thrombolysis (IVT).

Material and methods. We performed retrospective analysis of 362 AIS patients treated with IVT or IVT and subsequent mechanical thrombectomy in the University Hospital in Krakow, Poland. Patients were categorised into four subgroups by age: (I) below the age of 60, (II) 60 to 69, (III) 70 to 79, and (IV) 80 or more. The outcomes were assessed with modified Rankin scale (mRS) 90 days after stroke onset, and defined as favourable (mRS 0–2), poor (mRS 3–5), or death (mRS = 6).

Results. Patients aged 80 or more compared to those below 60 were more often women (72.64% vs. 26.76%, < 0.001), more often suffered from hypertension (94.34% vs. 60.56%, p < 0.001), ischaemic heart disease (27.36% vs. 8.45%, p = 0.002), atrial fibrillation (49.06% vs. 5.63%, p < 0.001), and premorbid disability (pre-stroke mRS ≥ 1: 17.92% vs. 1.41%, p < 0.001), less often were active smokers (0% vs. 27.14%, p < 0.001), more often had cardioembolic aetiology (50.00% vs. 16.90%, p < 0.001), and less often other stroke aetiology (1.89% vs. 15.49%, < 0.008), had shorter time from stroke onset to IVT (125 [93–180] vs. 140 [110–186] min, p < 0.008), less often underwent mechanical thrombectomy (18.87% vs. 46.48%, p < 0.001), had higher CRP levels (10.3 [3.2–39.8] vs. 4.3 [2.1–9.6] mg/L, p = 0.003), higher maximal systolic blood pressure within 24 hours after IVT (153 [140–170] vs. 138 [120–145] mmHg, p < 0.001), and higher creatinine concentration (88 [68–108] vs. 77 [67–87] µmol/l, p = 0.004), less often had a favourable outcome (48.04% vs. 85.51%, odds ratio [OR] 0.16, 95%CI: 0.07–0.34, p < 0.001), and had a greater risk of death (26.47% vs. 5.80%, OR 5.85, 95%CI: 1.95–17.59, p < 0.001) within three months of stroke onset. Multivariable logistic regression analysis showed that the independent predictors of worse outcome in patients aged 80 or more were NIHSS score after IVT (OR 0.64, 95%CI: 0.53–0.78, p < 0.001), pre-stroke mRS score ≥ 1 (OR 0.10, 95%CI: 0.02–0.61, p = 0.012), and CRP levels (OR 0.96, 95%CI: 0.93–0.99, p = 0.007).

Conclusions. AIS patients treated with reperfusion therapy and aged 80 or more have around a six times higher risk of an unfavourable outcome or death within three months of stroke onset compared to those aged below 60. Higher NIHSS score after IVT, any signs of disability before stroke as measured with mRS, and higher CRP levels are independent risk factors for worse prognosis in the elderly.

Key words: ischaemic stroke, intravenous thrombolysis, age, elderly, prognosis

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Introduction

Age is the most important non-modifiable risk factor for acute ischaemic stroke (AIS) [1]. Above the age of 45, stroke incidence doubles with each decade, and more than two-thirds of all cerebrovascular events occur after the age of 65 [2]. Due to the ageing population of Europe, increases in the incidence (+ 3%) and prevalence (+ 27%) of stroke are expected in the European Union over the next 30 years [3]. The COVID-19 pandemic additionally complicated the situation of patients with AIS, including the elderly, resulting in a significant decrease in the hospital admission rate and prolonged time to reperfusion therapies, especially during the first weeks of pandemic [4].

Data from a German stroke registry showed that the rate of treatment with intravenous thrombolysis (IVT) among patients with AIS decreased from 15% in those aged below 50 to 8% among those aged 90 or more [5]. Previous older studies showed that patients with AIS treated with IVT and aged 80 or more had three times higher three-month mortality compared to those below 80, with no significant difference in the rate of secondary symptomatic intracranial haemorrhage [6]. A recent Brazilian study revealed instead that, although patients with AIS treated with IVT or mechanical thrombectomy (MT) after the age of 80 had an increased risk of an unfavourable outcome when compared to younger individuals, the mortality rate was similar in all studied age subgroups [7]. Previous older studies have highlighted that the prevalence of cerebrovascular risk factors such as hypertension, diabetes mellitus, atrial fibrillation, and dyslipidemia is higher in the elderly, possibly leading to increased mortality and unfavourable outcomes in cases of AIS treated with IVT [8].

Therefore, the aim of our study was to assess the influence of age categorised into four subgroups on long-term functional outcomes in patients with AIS treated with IVT in a sample of the Polish population.

Material and methods

We retrospectively analysed the data of 362 patients with AIS treated with IVT between June 2014 and December 2018. Patient data was collected prospectively in the University Hospital in Krakow as part of a single-centre registry known as the Krakow Stroke Data Bank. Our study focused on age further categorised into four subgroups in a similar way as in the previous study of the Brazilian stroke cohort [7], i.e.: (I) below 60, (II) 60 to 69, (III) 70 to 79, and (IV) 80 or above.

The data on cardiovascular risk factors and outcome measures was collected as described previously [9]. In brief, we obtained information regarding demographics, pre-stroke modified Rankin scale (mRS), presence of hypertension, ischaemic heart disease, atrial fibrillation, diabetes mellitus, hypercholesterolemia, smoking habits, AIS aetiology, time from stroke onset to IVT, and National Institutes of Health Stroke Scale (NIHSS) recorded on admission and after IVT. C-reactive protein (CRP) levels were measured during the first 72 hours after hospital admission. Fasting glucose was measured in serum the next morning after IVT, as described previously [9]. The outcome was assessed with mRS 90 days after stroke onset, and was defined as favourable (mRS 0–2), poor (mRS 3–5), or death (mRS = 6). Secondary haemorrhagic brain complications caused by IVT were defined in accordance with the classification of the European Cooperative Acute Stroke Study (ECASS-1) [10].

This study received the approval of the Jagiellonian University Ethical Committee (KBET54/B/2007), and was conducted in accordance with the Declaration of Helsinki. Informed consent, either written or — in case of inability to use the dominant hand due to AIS — verbal in the presence of at least two physicians, was collected from each patient participating in the study.

The baseline clinical characteristics according to the age categories were presented as counts and percentages, median and interquartile range. The continuous data was tested for normality of distribution with a Shapiro-Wilk test. A Kruskal-Wallis test and test for multiple comparisons of mean rank were used to compare medians. Categorical variables were compared with the chi-square test and Fisher's exact test, and for pairwise comparisons, multiple hypothesis correction was performed using the Bonferroni method.

We performed logistic regression analysis to identify independent predictors of the 90-day outcome after AIS according to the age category. Multivariable models were built using backward stepwise elimination based on Akaike information criterion (AIC) levels. Models were adjusted for sex, NIHSS score, haemorrhagic brain complications after IVT, and CRP levels. The area under the receiver operating characteristic curve (AUC) with 95% confidence intervals (CI) was calculated to show the discriminative ability of the prediction models. All statistical tests were 2-sided, and a p-value of 0.05 was considered statistically significant. Data was analysed using STATISTICA version 13 (Statsoft Inc, Tulsa, OK, USA).

The data that confirms the results of the current study is available from the corresponding author upon reasonable request.

Results

Patient characteristics

Our study included 362 patients with AIS treated with IVT. One hundred and eight patients (29.8%) underwent also mechanical thrombectomy (MT). The prevalence of hypertension, atrial fibrillation, non-smoking, cardioembolic stroke aetiology and premorbid disability increased with each age category (Tab. 1). With increasing age categories, the chance of a favourable outcome gradually decreased, and the risk of death increased (Fig. 1).

Table 1. Baseline characteristics of patients according to age categories

	Age (years)				P-value
	< 60 years N = 71 (19.61%)	60–69 N = 81 (22.38%)	70–79 N = 104 (28.73%)	> 80 N = 106 (29.29%)	
Age [years]	51(42–56)	66 (64–68)	75 (72–77)	84 (82–87)	x
Women, n [%]	19 (26.76)	30 (37.04)	51 (49.04)*	77 (72.64)*†‡	< 0.001
BMI [kg/m^2]	27.3 (24.2–29.5)	26.8 (24.2–31.1)	26.7 (24.6–29.4)	26.5 (23.78–29.0)	0.373
Hypertension, n [%]	43 (60.56)	69 (85.19)*	92 (88.46)*	100 (94.34)*	< 0.001
Ischaemic heart disease, n [%]	6 (8.45)	17 (20.99)	32 (30.77)*	29 (27.36)*	0.004
Atrial fibrillation, n [%]	4 (5.63)	19 (23.46)*	31 (29.81)*	52 (49.06)*†‡	< 0.001
Diabetes mellitus, n [%]	12 (16.90)	25 (30.86)	35 (33.65)	33 (31.13)	0.071
Hypercholesterolemia, n [%]	26 (36.62)	23 (28.40)	37 (35.58)	31 (29.25)	0.545
Smoking, n [%]					
— active	19 (27.14)	26 (32.50)*	10 (9.80)*†	0 (0.00)*†‡	< 0.001
— past	17 (24.29)	12 (15.00)	18 (17.65)	13 (13.13)	
Previous stroke, n [%]	9 (12.68)	7 (8.64)	20 (19.23)	30 (28.30)†	0.028
Stroke aetiology, n [%]					
— large-vessel disease	8 (11.27)	9 (11.11)	23 (22.12)	9 (8.49)‡	0.022
— small-vessel disease	1 (1.41)	1 (1.23)	0 (0.00)	1 (0.94)	0.719
— cardioembolic	12 (16.90)	23 (28.40)	31 (29.81)	53 (50.00)*†‡	< 0.001
— other	11 (15.49)	2 (2.47)*	2 (1.92)*	2 (1.89)*	0.052
— undetermined	39 (54.93)	46 (56.79)	48 (46.14)	34 (38.68)	< 0.001
Time from stroke onset to thrombolysis [min]	140 (110–186)	118 (80–167)	145 (100–202)	125 (93–180)*	0.011
Mechanical thrombectomy, n [%]	33 (46.48)	31 (38.27)	24 (23.08)†	20 (18.87)*†	< 0.001
NIHSS score on admission	10 (6–18)	13 (6–18)	12 (6–18)	14 (6–18)	0.301
NIHSS score after r-tPA	5 (2–11)	6 (2–14)	5 (2–14)	8 (2–16)	0.335
Post-r-tPA haemorrhagic brain complications, n [%]					
— any haemorrhagic brain complication	16 (22.54)	21 (25.93)	15 (14.42)	23 (21.7)	0.255
— HI type 1	5 (7.00)	6 (7.41)	4 (3.85)	10 (9.43)	0.457
— HI type 2	6 (8.45)	9 (11.11)	4 (3.85)	5 (4.72)	0.176
— PH type 1	3 (4.23)	4 (4.94)	3 (2.88)	4 (3.77)	0.908
— PH type 2	2 (2.82)	2 (2.47)	4 (3.85)	4 (3.77)	0.941
Maximal SBP within 24 hours after r-tPA [mmHg]	138 (120–145)	143 (130–160)	147 (134-160)*	153 (140–170)*	< 0.001
Maximal DBP within 24 hours after r-tPA [mmHg]	80 (75–88)	80 (70–90)	80 (72-90)	80 (70–90)	0.983
Fasting glucose < 5.5 mmol/L	23 (32.39)	11 (13.58)	24 (23.08)	11 (10.38)	0.001
CRP [mg/L]	4.3 (2.1–9.6)	7.9 (3.0–20.0)	8.9 (3.6-37.1)*	10.3 (3.2–39.8)*†	0.002
Creatinine [µmol/L]	77 (67–87)	80 (67–96)	79 (69-100)	88 (68–108)*	0.007
Pre-stroke mRS					
— 0	70 (98.59)	78 (96.30)	96 (92.31)	87 (82.08)*†	0.001
— 1–2	1 (1.41)	2 (2.47)	4 (3.85)	15 (14.15)	
— 3–5	0 (0.00)	1 (1.23)	4 (3.85)	4 (3.77)	
Pre-stroke mRS score ≥ 1	1 (1.41)	3 (3.70)	8 (7.69)	19 (17.92)*†	< 0.001
mRS 0–1 90 days	53 (76.81)	50 (62.50)	61 (60.40)*	42 (41.18)*†‡	< 0.001
mRS 0–2 90 days	59 (85.51)	55 (68.75)*	68 (67.33)*	49 (48.04)*†‡	< 0.001
Death (mRS = 6)	4 (5.80)	9 (11.25)	14 (13.86)	27 (26.47)*	< 0.001

Bonferroni adjusted p-values: *P < 0.008, vs. <60 years; † P < 0.008, vs. 60–69 years; ‡ P < 0.008, vs. 70-79 years. Values are presented as n (%), median and interquartile range. BMI — body mass index; CRP — C-reactive protein; DBP — diastolic blood pressure; HI — haemorrhagic infarction; mRS — modified Rankin scale; MT — mechanical thrombectomy; NIHSS — National Institutes of Health Stroke Scale; PH — parenchymal haematoma; r-tPA — recombinant tissue plasminogen activator; SBP — systolic blood pressure

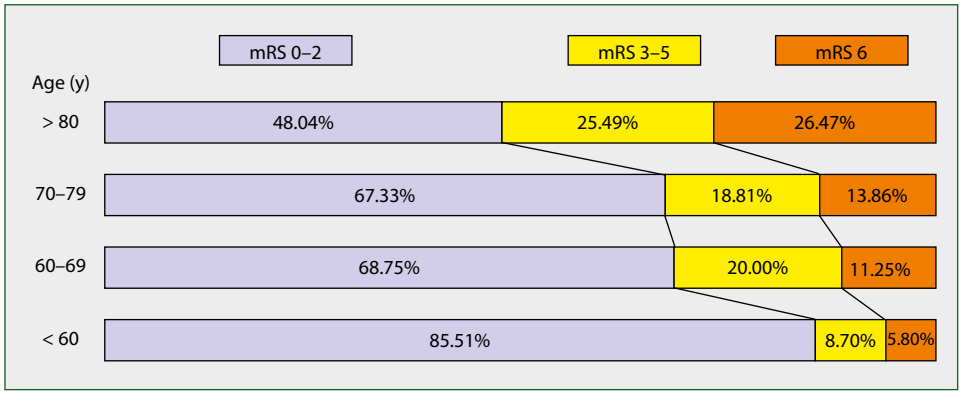

Figure 1. Proportions of patients with favourable outcome (modified Rankin scale [mRS] 0–2), poor outcome (mRS 3–5), and those who died (mRS = 6) three months after stroke onset, according to age categories

Comparison of age subgroups

Patients aged 80 or more (n = 106, median age 84 [82–87]) compared to those below 60 (n = 71, median age 51 [42–56]) were more often women, more often suffered from hypertension, ischaemic heart disease, atrial fibrillation and pre-stroke disability, less often were active smokers, more often had cardioembolic and less often other stroke aetiology, had shorter time from stroke onset to IVT, less often underwent MT, had higher CRP levels, higher creatinine concentration, and higher maximal systolic blood pressure within 24 hours after IVT, less often had favourable outcome (48.04% vs. 85.51%, p < 0.001), and had higher mortality 90 days after stroke onset (26.47% vs. 5.80%, p < 0.001) (Tab. 1, Fig. 1). Patients aged 80 or more had a more than six times higher risk of achieving mRS 3–6 90 days after stroke onset compared to those aged below 60 (OR 6.38, 95%CI: 2.94–13.84, p < 0.001) (Fig. 2).

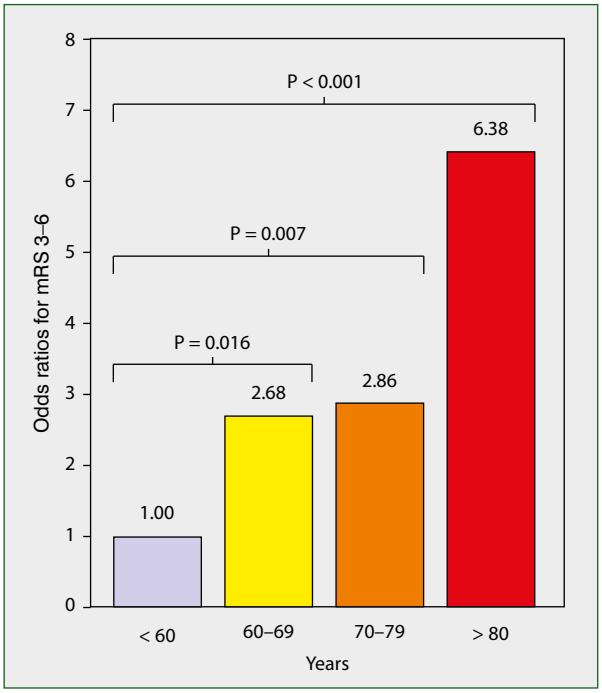

Figure 2. Odds ratios for modified Rankin scale 3–6 three months after stroke onset in studied age categories

Determinants of favourable outcome

Patients aged 80 or more who had mRS 3-6 90 days after stroke onset (n = 53) compared to those with favourable outcome (n = 49) had higher NIHSS score on admission (16 [14–20] vs. 7 [5–12], p < 0.001) and after IVT (15 [8–18] vs. 2 [1–6], p < 0.001), more often had haemorrhagic brain complications after IVT (35.85% vs. 8.16%, p < 0.001) and premorbid disability (pre-stroke mRS score ≥ 1: 28.30% vs. 8.16%, p = 0.010), less often had fasting glucose level below 5.5 mmol/L (9.43% vs. 26.53%, p = 0.023), had higher CRP levels (27.2 [9.1–84.1] vs. 4.3 [2.1–10.3] mg/L, p < 0.001), and had higher maximal diastolic blood pressure within 24 hours after IVT (80 [72–90] vs. 80 [70–85] mmHg, p = 0.026) (Supplemental Tab. 1). Patients below 60 who had mRS 3–6 90 days after stroke onset (n = 10) compared to those with a favourable outcome (n = 59) more often suffered from hypertension (90.00% vs. 54.24%, p = 0.033), more often underwent MT (90.00% vs. 38.98%, p = 0.028), had higher NIHSS score on admission (19 [18–20] vs. 9 [5–16], p = 0.005) and after IVT (19 [15–19] vs. 4 [2–8], p < 0.001), more often had haemorrhagic brain complications after IVT (70.00% vs. 14.56%, p < 0.001), and had higher CRP levels (9.3 [7.2–14.0] vs. 4.0 [1.5–7.7] mg/L, p = 0.018) (Supplemental Tab. 1).

More than two-thirds of patients with a pre-stroke mRS score of 0 experienced a favourable outcome 90 days after stroke onset, whereas 13% of patients without premorbid disability died during long-term observation (Supplemental Tab. 2). There were only nine patients with a pre-stroke mRS score of 3–5, and two of them died within 90 days of stroke onset (Supplemental Tab. 2).

Multivariable logistic regression analysis revealed that independent predictors of a favourable outcome were: lower

Table 2. Multivariable regression analysis for mRS 0–2 according to age categories

	< 60 years		60–69 years		70–79 years		> 80 years	
	OR (95% CI)	P-value	OR (95% CI)	P-value	OR (95% CI)	P-value	OR (95% CI)	P-value
Women	-	-	0.17 (0.04–0.82)	0.027	-	-	-	-
Pre-stroke mRS score ≥ 1	-	-	-	-	0.06 (0.01-0.58)	0.015	0.10 (0.02-0.61)	0.012
NIHSS score after r-tPA (per point)	0.68 (0.56–0.84)	< 0.001	0.73 (0.63–0.84)	< 0.001	0.68 (0.58–0.79)	< 0.001	0.64 (0.53–0.78)	< 0.001
Post-r-tPA haemorrhagic brain complications	-	-	-	-	-	-	-	-
CRP [mg/L]	-	-	-	-	-	-	0.96 (0.93–0.99)	0.007
AIC	32.91		52.91		54.89		63.67	
AUC (95% CI)	0.93 (0.87–0.99)		0.94 (0.89–0.99)		0.95 (0.91–0.99)		0.96 (0.93–0.99)	
Hosmer-Lemeshow test	0.152		0.945		0.027		0.410	

AIC — Akaike information criterion; AUC — area under receiver operating characteristic curve, CI — confidence intervals; OR — odds ratio

NIHSS score after IVT in all age subgroups, male sex in patients aged between 60 and 69, the lack of pre-stroke disability in patients aged 70 or more , and lower CRP levels in patients aged 80 or more (Tab. 2).

Patients treated with IVT and subsequent MT

Additional analyses were performed in the subgroup of patients restricted to those treated with IVT and subsequent MT. Patients aged 80 or more (n = 20, median age 83 [81–86]) compared to those below 60 (n = 33, median age 51 [42–55]) were more often women (90.00% vs. 21.21%, p < 0.001), more often suffered from hypertension (100.00% vs. 63.64%, p = 0.021), more often had cardioembolic aetiology (55.00% vs. 18.18%, p < 0.001), had shorter time from stroke onset to IVT (102 [73–129] vs. 143 [114–145] minutes, p = 0.012), and less often had a favourable outcome (31.58% vs. 71.88%, p = 0.012) (Supplemental Tab. 3, Supplemental Figure 1). In contrast to the whole group, there were no significant differences in patients aged 80 or more compared to those below 60 regarding CRP levels (11.4 [5.7–26.2] vs. 7.2 [2.6–11.0] mg/L, p = 0.237) or mortality 90 days after stroke onset (31.58% vs. 9.38%, p = 0.260). Patients aged 80 or more had a more than five times higher risk of achieving mRS 3–6 90 days after stroke onset compared to those below 60 (OR = 5.53, 95%CI: 1.61–19.07, p = 0.008) (Supplemental Figure 2).

Patients aged 80 or more who had mRS 3–6 90 days after stroke onset (n = 13) compared to those with a favourable outcome (n = 6) had a higher NIHSS score after IVT (15 [8–19] vs. 4 [2–10], p = 0.018) (Supplemental Tab. 4). However, there were no significant differences between the subgroups according to premorbid disability (pre-stroke mRS score ≥ 1: 30.77% vs. 0.00%, p = 0.255) or CRP levels (15.4 [7.1–27.4] vs. 10.1 [4.2–25.1] mg/L, p = 0.511) (Supplemental Tab. 4). Patients below 60 who had mRS 3–6 90 days after stroke onset (n = 9) compared to those with a favourable outcome (n = 23) had higher NIHSS score on admission (19 [18–20] vs. 16 [10–18], p = 0.015) and after IVT (19 [16–19] vs. 6 [3–11], p < 0.001) and more often had haemorrhagic brain complications after IVT (77.78% vs. 26.09%, p = 0.031) (Supplemental Tab. 4). Multivariable logistic regression analysis was not performed due to the small number of patients in the analysed subgroups.

Discussion

In our study, for the first time in a sample of Polish AIS patients we have evaluated stroke reperfusion therapy in four age categories: (I) below 60, (II) 60 to 69, (III) 70 to 79, and (IV) 80 or more. We were able to show that patients with AIS treated with IVT and aged 80 or more had a more than six times lower chance of a favourable outcome and a nearly six times greater risk of death within three months of stroke onset compared to those below 60. Our findings accord with a recent study performed on more than 500 rural residents of Poland that also revealed greater mortality and higher rate of functional dependence in thrombolysed patients aged 80 or more years compared to the remainder [11]. Similar conclusions came from a study of a Hungarian cohort comprising more than 1,000 AIS patients treated with IVT: this also showed a significantly lower chance of 1-year survival in the elderly [12]. Data coming from a previous systematic review of six studies including more than 2,000 AIS patients, among whom nearly one in four were aged 80 or more, also supported the results of our study [6]. In contrast, a recent study of a Brazilian cohort where patients treated with IVT and MT were analysed together showed that those aged 80 or more did not exhibit greater mortality, although they had less favourable outcomes at discharge and at three months after stroke onset [7].

Our study also revealed that elderly patients with AIS treated with IVT significantly more often were women, suffered from atrial fibrillation (AF), and had cardioembolic stroke aetiology. Our findings align with previous Hungarian research in which patients after the age of 80 had AF nearly three times as often as the remainder [12]. It is known that cardioembolic

stroke, most commonly caused by AF [13], is associated with increased long-term mortality compared to other aetiologies, even after adjustments for age and stroke severity [14]. Pooled analysis of more than 6,000 individuals with AIS showed also that women presented with more severe strokes. Although after adjustments for age and AF this association was attenuated, it still remained statistically significant [15]. Similarly, in a cohort of 1,830 Polish AIS patients treated with alteplase, women also exhibited worse long-term outcomes compared to men, probably due to their older age and higher frequency of cardioembolic stroke presenting with more severe neurological deficit [16].

When patients were analysed according to the mRS, it occurred that in all age subgroups worse outcome was associated with bleeding brain complications, CRP levels and NIHSS score, both on admission and after IVT. However, the multivariable model showed that NIHSS score after IVT was the only independent risk factor for worse outcome across all age subgroups. To date, studies have concentrated mainly on NIHSS score on admission [17, 18]. In a recent Italian study of nearly 500 AIS patients, higher NIHSS score was associated with an unfavourable outcome and the risk of death independently from treatment with IVT [19].

In the present study in patients aged 80 or more, higher CRP levels additionally were independently associated with worse functional outcome. As shown in our previous study, CRP levels evaluated in a different time window, i.e. 12-24 hours after IVT, were an independent risk factor for poor short-term and long-term outcomes and were also associated with in-hospital mortality [20]. Analysis of healthy individuals showed that people aged 65 or more had significantly higher CRP levels than their younger counterparts [21]. Moreover, CRP elevations in cases of stroke might reflect its severity [22]. Therefore, higher CRP levels, especially in the elderly, might play an important prognostic role in AIS treated with IVT. Previous studies have also suggested other potential risk factors for worse outcome of AIS in the elderly, such as antiplatelet or anticoagulant use before stroke, and higher white blood cell count [11]. A Chinese study showed that in older individuals with AIS, thrombolysis led to greater benefit in patients with lower NIHSS at baseline or those with posterior circulation infarct [23]. On the other hand, haemorrhagic brain complications were not found to be an independent risk factor for worse outcome in our study. Previous studies showed that the rate of intracerebral haemorrhage secondary to IVT, even when symptomatic, was similar in patients below and above the age of 80 [12]. Treatment with IVT significantly increased the number of patients with favourable outcome, defined as mRS of 0–2 at discharge in all age groups, including the elderly [5]. Even in patients after the age of 100, IVT could be efficiently used with no increase in the risk of secondary bleeding brain complications [24]. The same applied to those aged 90 or more years in the context of another type of reperfusion therapy, i.e. endovascular therapy, which did not increase the risk of symptomatic intracranial haemorrhage either [25].

Our study showed that premorbid disability, defined as pre-stroke mRS score of 1 point or more, was an independent risk factor for worse outcome in patients treated with IVT and aged 70 or more. Previous analysis of a large database from the Safe Implementation of Treatments in Stroke — Eastern Europe (SITS-EAST) registry revealed that a pre-stroke mRS score of 1 point or more was associated with an increased risk of death and a lower chance of favourable outcome within three months of a stroke treated with IVT [26]. Similar conclusions came from prospectively collected data from four major stroke centres in the United Kingdom [27]. Moreover, patients with premorbid disability were significantly older and had higher NIHSS score before IVT than the remainder [26, 28, 29]. Patients with premorbid disability were also less likely to improve within 24 hours after IVT [28]. On the other hand, a recent Italian study found that patients with pre-stroke disability, defined as mRS score of 3 or 4 treated with IVT, did not exhibit greater 3-month mortality compared to those who did not receive IVT even though thrombolysed patients were significantly older [30]. Another study showed that the benefit from thrombolysis depends rather on the patient's sex, and that this association is independent of pre-stroke mobility impairment [31].

When our analysis was restricted only to patients treated with IVT and subsequent MT, it occurred that in contrast to the whole group no significant differences were found between patients aged 80 or more and those below 60 regarding CRP levels and mortality 90 days after stroke onset. As the number of subjects included in this analysis is low, further studies are needed to evaluate whether other factors, such as NIHSS score after IVT, have a higher prognostic value. A previous Japanese study of patients who underwent MT showed that older age was not an independent risk factor for worse outcome, in contrast to NIHSS score and a modified Treatment in Cerebral Ischaemia (mTICI) score of 3 consistent with complete reperfusion [32]. Moreover, in patients aged 80 or more, the only predictive factor for worse outcome was an mTICI score of 3 [32]. A recent analysis of the 'MR CLEAN' trial (Multicentre Randomised Clinical Trial of Endovascular Treatment for Acute Ischaemic Stroke) revealed that patients aged 80 or more had worse functional outcome and increased mortality than younger patients, although older patients had a higher relative benefit of successful reperfusion [33].

Our study has some potential limitations. Firstly, the cohort of our AIS patients treated with IVT was rather small, although the median age value was distributed proportionally within the subgroups. Secondly, one-third of our patients underwent additional MT that could influence the results of our study, as elderly patients were less often qualified to this procedure and besides NIHSS score on admission did not differ from their younger counterparts. However, we performed additional analyses restricted to patients treated with IVT and subsequent MT. Finally, the results of the multivariable analysis need to be interpreted with caution, because due to

the small sample size only a few of the potential risk factors could be incorporated [34].

Conclusions

Our study demonstrates that AIS patients treated with IVT and aged 80 or more have about 6 times higher risk of unfavourable outcome or death three months after stroke onset compared to those aged below 60. Higher NIHSS score after IVT is an independent risk factor for worse prognosis in all age subgroups, whereas the prognostic significance of premorbid disability and of higher CRP levels is restricted to patients older than 70 and 80 years, respectively.

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