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Mechanical thrombectomy in very elderly people: short- and long-term outcomes of endovascular stroke treatment in nonagenarians

ABSTRACT

Aim of study. To assess outcomes of mechanical thrombectomy (MT) in nonagenarians suffering from acute ischaemic stroke (AIS) in a 1-year follow-up.

Clinical rationale for study. Age is a factor associated with both the occurrence of AIS and a poorer prognosis. As the population ages, the prevalence of AIS among the very old (90 and older) is expected to rise. Data on long-term outcomes of MT, being the optimal treatment of AIS caused by large vessel occlusions, is scarce in the population of nonagenarians.

Material and methods. We analysed all AIS patients treated with MT in a single Comprehensive Stroke Centre. We compared two subgroups: nonagenarians (people aged 90–99) and controls (< 90 years) in terms of cardiovascular risk factors profile, stroke severity, treatment course, presence of in-hospital complications, and outcomes (mortality and good functional outcome defined as modified Rankin Scale ≤ 2) at discharge and at 90- and 365-day follow-ups.

Results. Nonagenarians were more commonly female and suffering from atrial fibrillation. They more often developed urinary tract infection during hospitalisation. Stroke severity, treatment course and in-hospital outcomes were comparable between the groups. Nonagenarians had non-significantly higher 90-day and 365-day mortality, and a significantly lower rate of good functional outcomes after 90 days (25.0% vs 57.7%, $p = 0.011$) and 365 days (31.5% vs 61.0%, $p = 0.020$).

Conclusions and clinical implications. Despite worse outcomes than in younger patients, 25% of nonagenarians were functionally independent three months after MT, and almost one in three of them were so a year after the procedure, thereby showing the benefits of the treatment in this group.

Keywords: acute ischaemic stroke, mechanical thrombectomy, endovascular stroke treatment, age, nonagenarians

Introduction

The prevalence of cardiovascular diseases, including stroke, increases with age [1]. Among nonagenarians (people aged 90–99) features of a current or previous cerebrovascular

event can be found in as many as 20% in neuroimaging performed for any reason [2]. At the same time, life expectancy is growing and so the population of nonagenarians is expanding [3]. Therefore, clinicians these days are more often confronted with decision-making in acute ischaemic stroke

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(AIS) treatment in the very elderly. Older age predisposes towards worse short- and long-term AIS outcomes but is not the only factor independently associated with poor prognosis after stroke [4]. Studies suggest that the elderly may receive some forms of stroke prevention and acute phase management less often than do younger patients, due to scarce evidence regarding their safety in this group [5].

The European Stroke Organisation (ESO) guidelines give no upper age limit for qualification for reperfusion stroke therapies, neither intravenous thrombolysis (IVT) nor mechanical thrombectomy (MT) [6, 7]. The benefits of MT in the elderly were shown in a meta-analysis of five randomised control trials including 198 patients aged over 80 [8], but most evidence on the efficacy of MT in nonagenarians comes from smaller cohort studies [9–33]. Some researchers have suggested that in nonagenarians MT may be safer than IVT alone, resulting in a lower rate of intracerebral haemorrhage and a tendency towards better outcomes [34]. At the same time, age is one of the factors associated with poor functional outcomes even despite successful recanalisation [35]. Most experts advise individual decision-making, taking into account not only age, but the whole clinical picture.

Clinical rationale for study

More observations on MT outcomes in the elderly are needed, especially in long-term follow-ups. The aim of this study was to assess the clinical profiles, treatment course, complications and short- and long-term (up to 365 days after stroke onset) outcomes in nonagenarians treated with MT in the Comprehensive Stroke Centre (CSC) of the University Hospital in Kraków, Poland, and compare this against a younger population.

Material and methods

This study was a consecutive analysis of all MT-treated AIS patients hospitalised in the Comprehensive Stroke Centre of the University Hospital in Kraków, Poland, between 2019 and 2021. Qualification for reperfusion therapies was performed in accordance with the ESO guidelines [6]. Patients not treated with IVT and/or MT received standard medical treatment. Two subgroups were analysed: patients aged ≥ 90 (nonagenarians) and < 90 (controls).

We analysed the patients' sex and profile of cardiovascular risk factors: arterial hypertension, atrial fibrillation, diabetes mellitus, history of stroke or transient ischaemic attack (TIA), hypercholesterolemia, history of myocardial infarction, carotid artery atherosclerosis, peripheral artery disease, obesity, history of smoking and chronic kidney disease — definitions of particular risk factors are provided in a previous study from our Centre [36]. Stroke severity was defined as National

Institutes of Health Stroke Scale (NIHSS) score on admission to the CSC. Ischaemic lesion volumes (infarct core and penumbra) were estimated using computed tomography (CT) perfusion postprocessing analysis with an iRAPID program. We noted if the patient had been treated with IVT before MT. We assessed the time from stroke onset to groin puncture (SO-GP) and the time from groin puncture to reperfusion (GP-RP), as well as the number of device passages necessary to unblock the vessel. Successful reperfusion was defined as a modified Treatment in Cerebral Ischaemia (mTICI) score of 2B or 3. We noted the presence of intracerebral haemorrhage (ICH) after MT. We analysed the occurrence of medical complications i.e. pneumonia, urinary tract infection (UTI), malignant brain oedema, another stroke during hospitalisation, epileptic seizures, and venous thromboembolism (VTE). We noted hospital stay duration.

In-hospital outcomes were defined as transfer to the intensive care unit (ICU), in-hospital mortality, NIHSS score at discharge, and the presence of good functional outcome at discharge, defined as a modified Rankin Scale (mRS) score of ≤ 2 .

During scheduled visits in our Centre's outpatient clinic, or via telephone interviews with patients or their caregivers, we assessed mortality and the occurrence of a good functional outcome (mRS ≤ 2) 90 and 365 days after stroke onset.

The results were compared between nonagenarians and controls. Statistical analysis was performed using a PS Imago Pro 9.0 software. Categorical data was compared using a Chi-square test and continuous data with a U-Mann Whitney test (as the data distribution was other than normal, as proved using a Kolmogorov-Smirnov test). Continuous data was presented as medians and interquartile range (IQR). Two-tailed exact p-value of ≤ 0.05 was considered statistically significant.

The study was approved by the Jagiellonian University Ethical Committee (decision number 1072.6120.118.2020; 28.05.2020). Informed consent was not required. Financial support was given by the iBioStroke grant (Identification and clinical validation of biomarkers for long-term outcome after cerebral ischaemia, ERA-NET-NEURON/21/2020, K/NCB/00057) and Jagiellonian University Medical College grant (N41/DBS/000837).

Results

The study included 593 MT-treated AIS patients, of whom 16 (2.7%) were ≥ 90 years (range 90–97, median 91). The great majority of nonagenarians (87.5%) were women. Individual characteristics of nonagenarians are set out in Table 1.

Compared to controls, nonagenarians were much more commonly female (87.5% vs 46.4%, $p = 0.001$) and significantly more often suffered from atrial fibrillation (81.3% vs 41.1%, $p = 0.002$). There were no differences in the prevalence of other cardiovascular risk factors as well as the median sum of risk factors.

Table 1. Individual characteristics of MT-treated nonagenarians

Age, sex	Comorbidities	NIHSS score at admission	Penumbra and infarct volumes	IVT	SO-GP (min)	GP-RP (min)	mTICI	Complications	In-hospital outcome	90-day outcome	365-day outcome
1. 91, F	-	15	-	yes	230	45	3	pneumonia	NIHSS = 15 mRS=4	mRS = 6	mRS = 6
2. 93, F	AH, AF	21	penumbra = 41 ml infarct = 5 ml	yes	335	105	3	ICH	NIHSS = 14 mRS = 3	mRS = 6	mRS = 6
3. 93, F	AF, history of MI, CAA	9	-	yes	350	100	3	pneumonia, VTE	NIHSS = 0 mRS=2	mRS = 1	mRS = 1
4. 97, F	AH, AF, CKD	19	penumbra = 32 ml infarct = 0 ml	no	115	25	3	-	NIHSS = 0 mRS = 1	mRS = 5	mRS = 1
5. 94, F	AH, AF, history of stroke/TIA, PAD	8	penumbra = 25 ml infarct = 0 ml	no	290	40	3	-	NIHSS = 1 mRS=0	mRS = 0	mRS = 0
6. 91, F	AF, diabetes, obesity	14	penumbra = 109 ml infarct = 0 ml	yes	483	40	3	pneumonia, UTI	NIHSS = 18 mRS=5	mRS = 5	mRS = 5
7. 94, M	AH, AF, history of stroke/TIA,	21	penumbra = 51 ml infarct = 0 ml	yes	400	111	3	pneumonia, ICH	mRS = 6	mRS = 6	mRS = 6
8. 90, K	AF	16	penumbra = 133 ml infarct = 0 ml	no	175	70	2b	pneumonia, UTI, ICH	mRS = 6	mRS = 6	mRS = 6
9. 94, F	AH, AF, CKD	17	penumbra = 108 ml infarct = 12 ml	no	205	35	3	-	NIHSS = 5 mRS=4	mRS = 6	mRS = 6
10. 91, F	AH, AF	7	penumbra = 40 ml infarct = 5 ml	no	300	30	3	UTI	NIHSS = 4 mRS = 4	mRS = 1	mRS = 0
11. 91, F	AH, AF, CAA	12	penumbra = 199 ml infarct = 11 ml	yes	212	150	3	UTI	NIHSS = 8 mRS=5	mRS = 5	mRS = 6
12. 91, F	AH, AF	20	penumbra = 115 ml infarct = 59 ml	yes	265	45	2b	pneumonia, ICH	NIHSS = 8 mRS = 4	mRS = 6	mRS = 6
13. 90, M	AH	15	penumbra = 181 ml infarct = 0 ml	yes	275	50	3	-	NIHSS = 0 mRS = 1	mRS = 1	mRS = 1
14. 91, F	AH, AF, diabetes, hypercholesterolemia, history of stroke/TIA, obesity	17	penumbra = 135 ml infarct = 81 ml	no	299	49	3	UTI	NIHSS = 12 mRS = 5	mRS = 6	mRS = 6
15. 91, F	AH, diabetes, CKD	19	penumbra = 41 ml infarct = 0 ml	yes	305	23	2B	UTI	NIHSS = 8 mRS=4	mRS = 4	mRS = 4
16. 92, F	AH, AF, history of stroke/TIA,	20	penumbra = 89 ml infarct = 56 ml	no	138	31	3	pneumonia	NIHSS = 10 mRS=4	mRS = 4	mRS = 4

AF — atrial fibrillation; AH — arterial hypertension; CAA — carotid artery atherosclerosis; CKD — chronic kidney disease; GP-RP — groin puncture to reperfusion time; ICH — intracerebral haemorrhage; IVT — intravenous thrombolysis; MI — myocardial infarction; mTICI — modified Treatment in Cerebral Ischaemia scale; mRS — modified Rankin Scale; NIHSS — National Institutes of Health Stroke Scale; SO-GP — stroke onset to groin puncture time; TIA — transient ischaemic attack; UTI — urinary tract infection; VTE — venous thromboembolism

Median NIHSS score on admission did not differ between nonagenarians and controls. CT perfusion analysis results were available in 530 subjects (89.4%), with no significant differences in infarct core and penumbra volumes between the groups. Nonagenarians received treatment with IVT as often as controls (56.3% vs 57%, $p = 1.000$). The reasons for disqualification from IVT for seven nonagenarians were: oral anticoagulant intake in three patients, recent surgery in one, unknown precise time of stroke onset in one, a previous recent ischaemic stroke in one, and skin petechiae in one. SO-GP and GP-RP times were comparable. The decision on the form of anaesthesia (general anaesthesia vs conscious sedation) was made individually for each patient. In our nonagenarian cohort, 14 (87.5%) patients underwent conscious sedation and two (12.5%) needed general anaesthesia. The number of device passages was noted in 398 patients and there were no differences between the groups. Successful reperfusion was achieved in all nonagenarians (100.0% vs 87.5% of controls, $p = 0.240$). The occurrence of any intracranial bleeding was similar in both groups (25.0% vs 21.1%, $p = 0.756$). Nonagenarians more often than controls developed a UTI during hospitalisation (37.5% vs 15.8%, $p = 0.033$). There were no significant differences in the occurrence of other complications, nor the duration of hospital stay.

There were no significant differences between the groups in short-term outcomes, with similar rates of ICU transfers and in-hospital mortality (12.5% vs 13.7%, $p = 1.000$). The rate of good functional outcomes at discharge was lower (25% vs 49%) and median discharge NIHSS higher [8 (IQR=11) vs 4 (IQR=9)] in the nonagenarian group, but the results were not statistically significant ($p = 0.074$ and $p = 0.554$; respectively).

In our cohort of 16 MT-treated nonagenarians, there were no statistically significant differences in the in-hospital mortality or in the occurrence of good functional outcome at discharge between patients treated with IVT+MT vs MT only (14.3% vs 11.1%, $p = 1.000$ and 28.6% vs 22.2%, $p = 1.000$, respectively). Mean NIHSS score at discharge was higher in the IVT-treated subgroup, but the difference did not reach statistical significance (8.4 ± 6.2 vs 5.3 ± 4.8 , $p = 0.341$).

90- and 365-day follow-up was available in 97.5% and 93.9% of patients, respectively. Nonagenarians had non-significantly higher 90-day and 365-day mortality and a significantly lower rate of good functional outcomes after 90 days (25.0% vs 57.7%, $p = 0.011$) and after 365 days (31.5% vs 61.0%, $p = 0.020$).

A detailed comparison of the groups is set out in Table 2.

Discussion

The results of our study show that long-term functional outcomes of MT are worse among the very old than in the younger population. Nevertheless, 25% of nonagenarians were functionally independent three months after MT and almost

one in three of them a year after the procedure, thus showing the benefits of the treatment in the most elderly.

Effectiveness and safety of reperfusion therapies in elderly

Older age is known to be associated with worse prognosis after stroke [4]. Reperfusion therapies (RT) improve the outcomes of patients with AIS, including the elderly. Michelard et al. showed that treatment with IVT and/or MT is associated with a higher rate of early neurological improvement, an increased chance of good functional outcome at discharge, and lower in-hospital mortality in patients aged over 80 [9]. Gomes et al. retrospectively evaluated 3-month outcomes (mortality and disability) of nonagenarians undergoing RT (IVT and/or MT), and showed that they had similar outcomes as controls, but at the same time they also presented with a higher NIHSS score on admission and suffered from more haemorrhagic complications during hospitalisation [10]. Randomised control trials (RCTs) evaluating the efficacy of MT have not included many elderly patients, but a meta-analysis of individual patient data from five RCTs, including 198 patients aged over 80, has shown positive effects of the treatment (higher chance of functional independence after three months) in this subgroup [8]. Caruso et al. performed a retrospective analysis of the effectiveness of MT, narrowed to nonagenarians only, and in this study nine patients undergoing MT did not differ in discharge, 30-day or 90-day functional outcome compared to 33 who received standard medical care, although it has to be noted that the control group comprised all AIS patients, not only those with large vessel occlusions, so there is a risk of bias. MT-treated nonagenarians did not have an increased haemorrhagic complication rate compared to controls [11]. Wu et al. compared the effects of IVT and/or MT in nonagenarians; MT (with or without IVT) appeared to be safer in this population than IVT alone, resulting in a significantly lower rate of symptomatic intracranial haemorrhage [34]. There are case reports of successful MT even in 100-year-old patients [37].

Effects of MT in nonagenarians compared to younger populations

Cohort studies comparing MT-treated nonagenarians to younger patients mostly show no significant differences in successful recanalisation rates [12–19], SO-GP [12, 13, 15, 17], GP-RP [12, 15, 17], and the occurrence of haemorrhagic complications [12, 13, 15–17, 19]. In some there were no significant differences between the very old and controls concerning in-hospital mortality [15, 17, 18, 20] or functional status at discharge [14, 15, 17] and at 90-day follow-up [20]. Some others have reported a higher occurrence of symptomatic sICH [14], higher in-hospital mortality [14], worse in-hospital functional status (which was interestingly not confirmed in multivariate analysis) [18], a higher 90-day mortality rate [12, 16], and worse 90-day functional status [13, 16, 19] in nonagenarians. The differences in results are most probably a result of different

Table 2. Comparison of nonagenarians and controls

	Nonagenarians N = 16	Control group N = 577	P-value
Risk factors profile			
Female sex, [n (%)]	14 (87.5%)	268 (46.4%)	0.001
Arterial hypertension, [n (%)]	12 (75.0%)	401 (69.5%)	0.787
Atrial fibrillation, [n (%)]	13 (81.3%)	237 (41.1%)	0.002
Diabetes mellitus, [n (%)]	3 (18.8%)	122 (21.1%)	1.000
History of stroke/TIA, [n (%)]	4 (25.0%)	67 (11.6%)	0.113
Hypercholesterolemia, [n (%)]	1 (6.3%)	135 (23.4%)	0.137
History of myocardial infarction, [n (%)]	1 (6.3%)	74 (12.8%)	0.509
Carotid artery atherosclerosis, [n (%)]	2 (12.5%)	114 (19.8%)	0.551
Peripheral artery disease, [n (%)]	1 (6.3%)	57 (9.9%)	0.724
Obesity, [n (%)]	2 (12.5%)	114 (19.8%)	0.551
History of smoking, [n (%)]	0 (0.0%)	124 (21.5%)	0.054
Chronic kidney disease, [n (%)]	3 (18.8%)	56 (9.7%)	0.389
Sum of cardiovascular risk factors, [median (IQR)]	3 (IQR = 1)	2 (IQR = 3)	0.792
Stroke characteristics			
Infarct volume (ml), [median (IQR)], N = 530	2.5 (IQR = 23)	7 (IQR = 26)	0.470
Penumbra volume (ml), [median (IQR)], N = 530	98.5 (IQR = 93)	89 (IQR = 75)	0.968
NIHSS score on admission, [median (IQR)]	16.5 (IQR = 7)	16 (IQR = 9)	0.590
Treatment course			
Intravenous thrombolysis, [n (%)]	9 (56.3%)	329 (57.0%)	1.000
SO-GP, [median (IQR)]	282.5 (IQR = 120.75)	295 (IQR = 145)	0.346
GP-RP, [median (IQR)]	45 (IQR = 60.5)	60 (IQR = 45)	0.078
Device passages, [median (IQR)], (N = 398)	2 (IQR = 2)	1 (IQR = 2)	0.638
Successful reperfusion, [n (%)]	16 (100.0%)	504 (87.5%)	0.240
Intracranial haemorrhage, [n (%)], N = 566	4 (25.0%)	122 (21.1%)	0.756
Hospital stay duration (days), [median (IQR)]	10 (IQR = 7)	9 (IQR = 4)	0.319
Medical complications			
Pneumonia, [n (%)]	7 (43.8%)	152 (26.3%)	0.150
Urinary tract infection, [n (%)]	6 (37.5%)	91 (15.8%)	0.033
Malignant oedema, [n (%)]	0 (0.0%)	22 (3.8%)	0.657
Another stroke during hospitalisation, [n (%)]	0 (0.0%)	8 (1.4%)	1.000
Epileptic seizures, [n (%)]	0 (0.0%)	2 (0.3%)	1.000
Venous thromboembolism, [n (%)]	1 (6.3%)	9 (1.6%)	0.241
In-hospital outcomes			
ICU transfer, [n (%)]	2 (12.5%)	55 (9.5%)	1.000
In-hospital mortality, [n (%)]	2 (12.5%)	79 (13.7%)	1.000
NIHSS score at discharge, [median (IQR)]	8 (IQR=11)	4 (IQR=9)	0.554
Good functional outcome at discharge, [n (%)]	4 (25.0%)	283 (49.0%)	0.075
90-day outcomes (N = 578)			
90-day mortality, [n (%)]	7 (43.8%)	126 (22.4%)	0.066
90-day good functional outcome, [n (%)]	4 (25.0%)	324 (57.7%)	0.011
365-day outcomes (N = 557)			
365-day mortality, [n (%)]	8 (50.0%)	165 (30.5%)	0.106
365-day good functional outcome, [n (%)]	5 (31.5%)	330 (61.0%)	0.020

ICU — intensive care unit; IQR — interquartile range; NIHSS — National Institutes of Health Stroke Scale; TIA — transient ischaemic attack

study designs. Interestingly, Khan et al. reported that although 90-day functional outcomes were worse among patients ≥ 90 , at the same time they had higher pre-stroke mRS and there was no difference between nonagenarians and controls in the rate of mRS change from before stroke to 90 days after stroke [19]. Higher pre-stroke mRS among nonagenarians compared to younger controls was also reported by other studies [13, 17, 19, 21]. Rotschild et al. observed that nonagenarians with significant pre-stroke disability had worse outcomes than those with baseline mRS ≤ 3 [13], and pre-stroke mRS was also associated with 3-month functional outcome in a study by Derraz et al. [22]. Unfortunately, we did not have access to the information about pre-stroke functional status in our group, which is a significant limitation of our analysis.

Some researchers have compared the outcomes of MT between nonagenarians and octogenarians (aged 80-89). Results include higher nonagenarian mortality, both in-hospital [9] and in 3-month follow-up [12, 23], but no differences in functional status at discharge [21] or 90 days after stroke [23-25]. One study reported an increased risk of symptomatic ICH in nonagenarians compared to octogenarians [23].

Bai et al. [38] published a systematic review with meta-analysis including 13 cohort studies and 657 MT-treated nonagenarians. In this group, the successful recanalisation rate was 80.82%, the rate of iCH was 12.8% (with symptomatic ICH in 3.5%), in-hospital mortality was 20.6% (44.4% in 3-month observation), and good functional outcome at discharge was achieved in 21.6% of patients. Our study showed a higher percentage of successful reperfusion and better in-hospital outcomes, but also a higher rate of ICH. These differences may be a result of the size of our sample.

Our observations concerning some differences between nonagenarians and younger patients were also previously noted by other researchers, including higher female sex prevalence [13, 16-18, 20], higher co-occurrence of atrial fibrillation [19, 20], and more common occurrence of UTI during hospitalisation [18].

Factors associated with MT outcomes in nonagenarians

Various studies have identified factors associated with outcomes of MT among nonagenarians. Kawaji et al. found NIHSS score at admission to be a predictor of functional status at discharge, whereas age was not [17]. Similarly, in a study by Andrews et al., functional outcome at discharge was associated with IVT, successful reperfusion, NIHSS score on admission, and UTI during hospitalisation, but not with age [18]. Rahangdale et al. observed that nonagenarians surviving until discharge had smaller infarct core volumes than those who died in hospital [14]. In a study by Tonetti et al., final infarct volume of less than 10 cm³ strongly predicted patient discharge home [26]. Factors associated in different studies with favourable 90-day mRS in MT-treated nonagenarians included age [19, 27], pre-stroke mRS [22, 27], NIHSS score

on admission [10, 19, 28, 39], Alberta Stroke Program Early CT Score (ASPECTS) on admission [39], good collaterals [29], successful recanalisation [19, 22, 30], early neurological improvement [22], the presence of any intracranial haemorrhage [28], and in-hospital respiratory infection [10]. In a study by Sojka et al., patients with favourable 3-month outcomes (mRS 0-2) had significantly lower NIHSS score on admission, shorter onset to arrival time, less prevalent tandem occlusions, lower rate of large vessel disease stroke aetiology, and were less frequently treated with statins and antihypertensive medications before stroke onset [31]. In a study by Drouard-de-Rousiers et al., 3-month mortality after MT in nonagenarians was associated with successful reperfusion after the first pass of the device [30], and, in the study by Derraz et al., with early neurological improvement [22]. In some studies, no independent factors associated with good functional outcome at 90 days [32] or in-hospital mortality [33] were found. In our study, the sample size was unfortunately too small to perform multivariate analyses identifying factors associated with nonagenarians' outcomes, which is another limitation.

Despite the abovementioned flaws, the strength of our study is the long-term follow-up, with observations up to 365 days available in 93.9% of patients.

Clinical implications

The very old are a frail population, prone to worse outcomes of stroke treatment, including MT. At the same time, age is not the only factor associated with a worse prognosis, and other factors play an important role, such as pre-stroke disability, stroke severity, infarct volume, good collaterals, and successful recanalisation. In our study, significant numbers of nonagenarians achieved functional independence (almost one third in a year-long observation). Therefore, clinicians should not disqualify patients from MT based on age alone.

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