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Kortelainen, Simon

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## RESEARCH ARTICLE

# Acute ischemic stroke in a university hospital intensive care unit: 1-year costs and outcome

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## Abstract

**Background and purpose:** Little is currently known about the cost-effectiveness of intensive care of acute ischemic stroke (AIS). We evaluated 1-year costs and outcome for patients with AIS treated in the intensive care unit (ICU).

**Materials and methods:** A single-center retrospective study of patients admitted to an academic ICU with AIS between 2003 and 2013. True healthcare expenditure was obtained up to 1 year after admission and adjusted to consumer price index of 2019. Patient outcome was 12-month functional outcome and mortality. We used multivariate logistic regression analysis to identify independent predictors of favorable outcomes and linear regression analysis to assess factors associated with costs. We calculated the effective cost per survivor (ECPS) and effective cost per favorable outcome (ECPFO).

**Results:** The study population comprised 154 patients. Reasons for ICU admission were: decreased consciousness level (47%) and need for respiratory support (40%). There were 68 (44%) 1 year survivors, of which 27 (18%) had a favorable outcome. High age (odds ratio [OR] 0.95, 95% confidence interval [CI] 0.91–0.98) and high hospital admission National Institutes of Health Stroke Scale score (OR 0.92, 95% CI 0.87–0.97) were independent predictors of poor outcomes. Increased age had a cost ratio of 0.98 (95% CI 0.97–0.99) per added year. The ECPS and ECPFO were 115,628€ and 291,210€, respectively.

**Conclusions:** Treatment of AIS in the ICU is resource-intensive, and in an era predating mechanical thrombectomy the outcome is often poor, suggesting a need for further research into cost-efficacy of ICU care for AIS patients.

## KEYWORDS

acute ischemic stroke, cost of care, cost-efficacy, intensive care

Markus B. Skrifvars reports lecture fees and travel grants from BARD Medical (Ireland).

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### Editorial Comment

This report investigates the cost of intensive care for patients with acute ischaemic stroke in the era before mechanical thrombectomy. It sets an important Scandinavian baseline against which to compare the costs of intensive care for these patients after the introduction of mechanical thrombectomy.

## 1 | INTRODUCTION

Stroke is the second most common cause of death and the third most common cause of lost disability-adjusted life years worldwide.<sup>1,2</sup> Stroke encompasses two entities of which acute ischemic stroke (AIS) is the more common, constituting about 75%–80% of all strokes.<sup>3</sup> About 15%–20% of patients admitted to a stroke unit develop the need for care in an intensive care unit (ICU).<sup>4</sup> Common indications include decreased consciousness, the need for mechanical ventilation or intensive hemodynamic management, and invasive neurological or systemic monitoring.<sup>5</sup> Other possible indications are the need for monitoring given massive infarctions with risk to herniation requiring surgery, seizures, and status epilepticus.<sup>4,5</sup> ICU care for patients focuses on short-term organ support including management of the airways and ventilation, hemodynamical support, and treatment of fever, dysglycemia, and control of seizures.<sup>6</sup> Long-term mortality of ICU-admitted AIS patients is nonetheless high, ranging from 37% to 66% mortality at 1 year, and with only 8%–14% surviving with good functional outcomes.<sup>7–12</sup> Known predictors of mortality in the ICU setting include the need for mechanical ventilation and decreased level of consciousness on admission.<sup>13</sup>

The economic burden of stroke is immense. In Finland, the annual expenditure has been estimated at 1.1 billion euros.<sup>14</sup> Reported data about costs specific to AIS requiring ICU treatment are scarce, and thus, little evaluation of cost efficacy has been made. Accordingly, our primary aim in the current study was to assess 1-year costs of care for ICU patients with AIS. In addition, as secondary aims were to evaluate cost-efficacy, the reasons AIS patients require ICU admission and whether this influences the long-term prognosis and cost-effectiveness of ICU care. Our hypothesis was that the cost-efficacy of ICU care overall is low and that the efficacy would further decrease when the age of the patients increase.

## 2 | MATERIALS AND METHODS

### 2.1 | Setting

We conducted a retrospective observational study of patients with AIS admitted to a tertiary academic ICU between 2003 and 2013. Meilahti Hospital is a publicly funded hospital in the Helsinki-Uusimaa region with a catchment area of approximately 2.2 million people and the primary referral center for patients with AIS in need of thrombolysis or mechanical thrombectomy (MT). The Finnish

National Institute for Health and Welfare (THL/2034/5.05.00/2017) approved this study and waived the need for informed consent.

### 2.2 | Variables and data sources

From the Finnish Intensive Care Consortium (FICC) database, we extracted adult patients (aged  $\geq 18$ ) treated for AIS at the ICUs of Helsinki University Hospital from 1 January 2003 through 31 December 2013, identified from the database based on their Acute Physiology and Chronic Health Evaluation III (APACHE III) diagnosis. This data were extracted as a part of a set of studies reported earlier.<sup>15,16</sup> Individual-level healthcare records were subsequently used to confirm the diagnosis of AIS. Location of ischemic lesion was identified and classified into supra- or infratentorial stroke, or both. Stroke severity on admission to the hospital was evaluated using a National Institutes of Health Stroke Scale (NIHSS) score when absent in admission status records, and functional status at 12 months was evaluated using modified Rankin Scale (mRS).<sup>17,18</sup> The evaluation of stroke-location, NIHSS, and mRS were made by a senior house officer in neurology with adequate training and experience by reviewing individual-level healthcare records. In addition, the medical records were reviewed for the indication for ICU admittance and interventions undergone. The admission reasons were classified according to indications reported in earlier literature. When no suitable group existed, a new one was formed. These were then regrouped into four main indications reported in Table 1.

In addition, from the FICC database, we obtained data regarding the Therapeutic Intervention Scoring System (TISS-76), APACHE II, Simplified Acute Physiology Score (SAPS) II, Sequential Organ Failure Assessment (SOFA), World Health Organization/Eastern Cooperative Oncology Group (WHO/ECOG) performance status before incident, and length of stay (LOS) in the ICU and hospital. Dates of death were extracted from the Finnish Population Register Centre database using social security numbers.

### 2.3 | Cost data

Patients' social security numbers were used to obtain data about university hospital, rehabilitation, and social security costs at 1 year from incidence. University hospital costs were from the treatment period as noted in the billing records, including, for example, personnel, diagnostics, and hospital stay. Rehabilitation costs were estimated by multiplying the length of stay (days) at the rehabilitation center with the average cost of stay per day at a center with a

TABLE 1 Detailed baseline characteristics of patients included in the study, grouped according to outcome

Baseline patient characteristics		All subjects	Outcome (mRS), n		p-value
			Good (0–2), 27	Poor (3–6), 127	
Age, years, median (IQR)		68 (60–75)	62 (52–71)	69 (61–75)	.006
Sex, n (%)	Male	98 (64)	19 (70)	79 (62)	.512
WHO/ECOG performance status, n (%)	Fit for work or equal	115 (80)	22 (81)	93 (73)	.495
	Unfit for work, independent in self-care	16 (11)	1 (4)	15 (12)	
	Partially dependent in self-care	12 (8)	2 (7)	10 (8)	
Severe comorbidity at admission (according to SAPS II or APACHE II <sup>a</sup> ), n (%)		14 (9)	1 (4)	13 (10)	.466
GCS <sup>b</sup> , n (%)	3–8	101 (67)	14 (54)	87 (70)	.147
	9–12	23 (15)	4 (15)	19 (15)	
	13–15	27 (18)	8 (31)	19 (15)	
NIHSS at admission, median (IQR)		19 (10–28)	10 (6–18)	22 (13–30)	.001
NIHSS at admission <sup>c</sup> , n (%)	0–4	12 (8)	4 (15)	8 (6)	.012
	5–15	49 (32)	14 (54)	35 (28)	
	16–20	18 (12)	2 (8)	16 (13)	
	21–42	73 (48)	6 (23)	67 (53)	
Infarction site <sup>c</sup> , n (%)	Supratentorial	84 (55)	9 (33)	75 (59)	.044
	Infratentorial	60 (40)	14 (52)	46 (36)	
	Both	8 (5)	3 (11)	5 (4)	
Primary reason for ICU admittance, n (%)	Respiratory support <sup>d</sup>	61 (40)	12 (44)	49 (39)	.575
	Decreased conscious level or sedation <sup>e</sup>	72 (47)	11 (41)	61 (48)	
	Organ support and hemodynamic management	15 (10)	2 (7)	13 (10)	
	Other, nonmedical	6 (4)	2 (7)	4 (3)	
Intervention, n (%)	Noninvasive care	81 (60)	14 (52)	67 (53)	.551
	Thrombolysis	45 (33)	7 (26)	38 (30)	
	Thrombectomy	9 (7)	0 (0)	9 (7)	

Abbreviations: IQR, Interquartile range; mRS, modified Rankin Scale; WHO/ECOG, World Health Organization/Eastern Cooperative Oncology Group; SAPS, Simplified Acute Physiology Score; APACHE, Acute Physiology and Chronic Health Evaluation; GCS, Glasgow Coma Scale; NIHSS, National Institutes of Health Stroke Scale; ICU, intensive care unit.

<sup>a</sup>SAPS II: Metastatic cancer, hematologic malignancy, AIDS. APACHE II: New York Heart Association Heart Failure Class IV, cirrhosis, chronic lung disease, immunocompromised or dialysis dependent.

<sup>b</sup>N = 151.

<sup>c</sup>N = 152.

<sup>d</sup>Mechanical ventilation due to aspiration, oxygen supplementation, or lower cranial nerve impairment.

<sup>e</sup>Sedation due to seizure or low co-operation.

similar level of care. Social security costs were obtained from the Finnish Social Security Institute and included private doctor and physiotherapist fees, costs of prescribed medication, disability and sickness allowances, and costs of medically related transport. An example cost-calculation is available as a digital supplement.

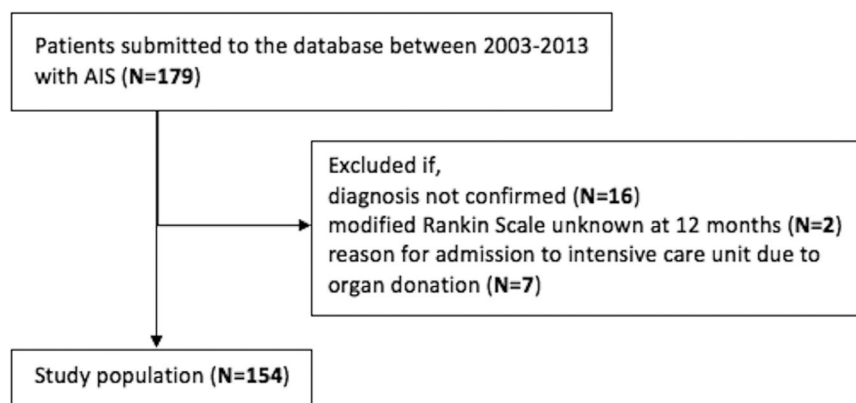
The costs were adjusted to the consumer price index (CPI) of 2019. CPI data were obtained from Statistics Finland, a national public authority on statistics.<sup>19</sup> The adjustment was done using the following formula:

$$\text{CPI 2019 adjusted costs} = \text{Costs} \times \frac{\text{CPI 2019}}{\text{CPI of admission year}}$$

## 2.4 | Outcome

As the primary outcome examined was cost of care at 1 year as specified above. As secondary outcomes examined were functional outcome and all-cause mortality at 12 months. A favorable functional outcome was defined as an mRS score of 0–2 (from no symptoms to slight symptoms but can take care of one's own affairs without assistance) and an unfavorable outcome as an mRS score of 3–6 (needing assistance at times to needing constant nursing assistance or death). Based on the functional outcome and mortality, we calculated the effective cost per survivor (ECPS) and effective cost per favorable

FIGURE 1 Flowchart describing selection of study population



outcome (ECPFO) as detailed below. We also report in-ICU and in-hospital mortality rates.

## 2.5 | Statistical analysis

We used SPSS Statistics for MacOS version 25.0 (IBM Corp, Armonk, NY) for analysis. Due to some small sample sizes, Fisher's exact test was used for comparison between categorical variables. Due to skewness and kurtosis of data, continuous variables are reported as medians with interquartile ranges (IQR). For continuous nonparametric data, a Mann-Whitney U-test was used. A univariate logistic regression analysis was conducted to examine the predicted variables of favorable outcomes at 1 year. We constructed multivariable logistic regression models for the assessment of independent variables affecting the outcome, and these were reported as odds ratios (OR) for a good outcome with corresponding 95% confidence intervals (CI). Where appropriate, bootstrapping with bias correlated acceleration was used. A linear regression analysis was conducted to identify and quantify factors independently associated with costs. Due to skewness and heteroscedasticity, a log-transformation of the cost data was done before the linear regression analysis. The results were then exponentiated, resulting in cost ratios: a cost ratio of 1.05 indicates that a one-unit increase of a variable increased costs by 5%. The variables were analyzed in a univariate analysis and significant results ( $p < 0.05$ ) were added to a multivariate analysis. This procedure was done for the whole study population and repeated for the hospital survivors subgroup.

The average cost per hospital day per patient was obtained by dividing the total university hospital costs by the LOS in hospital. The medians with IQR are reported. ECPS and ECPFO were calculated by dividing the total healthcare associated costs by the number of 1-year survivors and the number of patients with a favorable neurological outcome, respectively. The ECPS and ECPFO were also stratified by stroke severity using the NIHSS score into the following groups: no stroke or minor stroke (0–4), moderate stroke (5–15), moderate to severe stroke (16–20), and severe stroke (21–42).

## 3 | RESULTS

### 3.1 | Study population

Between 2003 and 2013, approximately 1200 AIS patients were admitted annually to Meilahti Hospital.<sup>20,21</sup> During the period, 179 patients were admitted to the ICU with AIS as a primary or secondary diagnosis. Of these, 25 patients were excluded due to insufficient data, loss to follow-up, or admission to ICU as an organ donor (Figure 1). Baseline characteristics of the included patients are presented in Table 1. Of the patients admitted, 67% had a low (3–8) presenting Glasgow Coma Scale (GCS). The median presenting NIHSS score was 19 (IQR 10–28), indicating a moderate to severe stroke. The patients with favorable outcomes were younger and more commonly had an infratentorial stroke. No significant difference in the pre-admission WHO/ECOG performance status was observed between the outcome groups. The patients were mostly admitted to ICU due to decreased consciousness level or need for sedation (47%), or need of respiratory support (40%).

### 3.2 | Outcome

The in-ICU mortality was 14%, in-hospital mortality 36%, and 1-year mortality 56%. Of the 1-year survivors, 40% (or 18% of all patients) had a good neurological outcome. Admission NIHSS was significantly lower in the group with favorable outcomes than the group with unfavorable outcomes (median 10 [IQR 6 – 18] vs 22 [IQR 13 – 30],  $p = 0.001$ ). The indications for ICU admission were similar in the two outcome groups.

In the logistic regression analysis, age, admission NIHSS score, and the location of infarction were independently associated with outcome (Table 2); supratentorial location of infarction reduced the likelihood of a good outcome the most (OR 0.367 [95% CI 0.141–0.957]), followed by NIHSS (OR 0.918 [95% CI 0.874–0.965]), and age (OR 0.945 [95% CI 0.911–0.981]). Interestingly, WHO/ECOG performance status was not independently associated with outcome.

TABLE 2 Logistic regression analysis of independent predictors of favorable outcome

Predictors of favorable outcome <sup>c</sup>				
Variable	Univariate odds ratio (95% CI <sup>d</sup> )	p-value <sup>d</sup>	Multivariate odds ratio (95% CI <sup>d</sup> )	p-value <sup>d</sup>
Age <sup>a</sup>	0.952 (0.922–0.983)	.002	0.945 (0.911–0.981)	.001
NIHSS <sup>b</sup>	0.925 (0.883–0.970)	.004	0.918 (0.874–0.965)	.002
Infarct location				
Supratentorial	0.360 (0.149–0.870)	.023	0.367 (0.141–0.957)	.040
Infratentorial or both	Reference		Reference	
WHO/ECOG performance status				
Independent	Reference		Excluded from analysis	
Independent in self-care but unable to work	0.282 (0.035–2.249)	.117	Excluded from analysis	
Partially dependent in self-care	0.845 (0.173–4.136)	.706	Excluded from analysis	

Abbreviations: CI, Confidence Interval; WHO/ECOG, World Health Organization/Eastern Cooperative Oncology Group.

<sup>a</sup>Defined as modified Rankin Scale 0–2.

<sup>b</sup>Based on Bias Correlated bootstrap with 1000 samples.

<sup>c</sup>Every step increases age by a year.

<sup>d</sup>Every step increases National Institutes of Health Stroke Score (NIHSS) by one.

### 3.3 | Resource use and treatment intensity

Variables representing resource use and treatment intensity are presented in Table 3. Severity of illness scores differed significantly between the favorable and unfavorable outcome groups, being 21 (IQR 13–25) vs 25 (IQR 20–29) for APACHE II and 44 (IQR 32–51) vs 56 (IQR 41–63) for SAPS, respectively. The groups were similar with regards to need for care according to TISS-76 (daily average or maximal), stroke interventions, LOS at hospital and ICU, or time between hospital admission and ICU admission.

### 3.4 | Healthcare-associated costs, cost-effectiveness, and factors influencing healthcare-associated costs

The total cost of patient care was 7,862,675€. Of the total cost, 54% was from university hospital expenses, 10% from social security expenses, and 36% from rehabilitation expenses. Notably, of the total expenses, only 26% were used on patients with favorable neurological outcomes at 1 year.

The median average cost per day in hospital care was 1,578€ and the mean total cost per patient was 51,390€ for the whole study population. The median total cost was significantly higher in the favorable outcome group, as can be seen in Table 3. The ECPS was 115,628€ and ECPFO was 291,210€. Figure 2 illustrates the change in EPCS and ECPFO according to stroke severity.

Variables associated with costs of patient care are presented as cost ratios in Table 4. In the whole study population, an increase in age and APACHE and SAPS scores was associated with lower costs, and maximal TISS and LOS at hospital or ICU were associated with higher costs in univariate analyses. In the multivariate analysis, the

only significant predictor of costs that remained was LOS at hospital; an increase in the hospital stay for 1 day had a cost ratio of 1.04 (95% CI 1.03–1.05). In the hospital-survivors subgroup, increasing age was associated with lower costs, and maximal TISS score and length of hospital or ICU stay were associated with higher costs in univariate analyses. Notably, in the multivariate analysis, only age significantly predicted cost; a 1-year increase in age at incident had a cost ratio of 0.98 (95% CI 0.97–0.99), i.e. decreased the costs by 2%.

Figure 3 describes the difference in mean costs according to functional outcome and time of death. The cost of rehabilitation was significantly lower for the 1-year survivors with favorable outcomes than those with unfavorable neurological outcomes.

## 4 | DISCUSSION

### 4.1 | Key results

In this single-center retrospective study of AIS patients treated between 2003 and 2013, ICU care had high healthcare costs, and only one-fifth of the patients recovered enough to gain independence. With increasing stroke severity, cost efficacy clearly declined. For the moderate to severe stroke group, the ECPFO was nearly three times as high as the ECPS and more than three times the ECPFO in the no stroke to minor stroke group. This study highlights the need for better prognostic tools for clinicians admitting AIS patients to ICU care, and in the meantime, for critical evaluation of ICU admittance rationale in hospitals. Nonetheless when interpreting these results we need to take into the consideration the substantial advancement in both stroke and intensive care in recent years, especially the implementation of MT and thrombolysis into mainstream practice.<sup>22</sup>

TABLE 3 Resource use, intensive care unit (ICU) interventions, and costs

Resource use and outcome					
Variable		All subjects (N = 154)	Outcome (mRS), n		p-value
			Good (0–2), 27	Poor (3–6), 127	
TISS-76, median (IQR)	Daily average	27 (25–31)	28 (25–30)	27 (25–31)	.781
	Total	67 (50–128)	87 (51–131)	64 (50–125)	.179
	Daily average	27 (25–31)	28 (25–30)	27 (25–31)	.781
	Total	67 (50–128)	87 (51–131)	64 (50–125)	.179
TISS interventions undergone, n (%)	Mechanical ventilation	137 (89)	23 (85)	113 (89)	1.000
	Hemodialysis	2 (1)	0 (0)	2 (2)	1.000
	Emergency operation	4 (3)	1 (4)	3 (2)	.541
	Vasoactive medication	111 (72)	18 (67)	93 (73)	.487
	Anticoagulation	122 (79)	24 (89)	98 (77)	.203
Length of stay, days, median (IQR)	Hospital	11 (3–22)	14 (10–22)	10 (2–22)	.099
	ICU	2 (1–4)	2 (1–4)	2 (1–3)	.147
Time from hospital admission to ICU admission, days, median (IQR)		1 (1–1)	1 (1–2)	1 (0–1)	.204
APACHE II score, median (IQR)		24 (19–29)	21 (13–25)	25 (20–29)	.006
SAPS II, median (IQR)		53 (38–62)	44 (32–51)	56 (41–63)	.002
SOFA score, median (IQR)		8 (6–10)	8 (6–10)	8 (6–10)	.664
Costs at 1 year, 2019 euro, median (IQR)	Total	35 393 (12 614–74 056)	61 663 (42 628–92 364)	28 773 (11 078–67 137)	.001
	University hospital <sup>a</sup>	19 803 (9880–35 955)	27 022 (18 211–53 907)	16 822 (7563–32 186)	.004
	Social security <sup>b</sup>	1209 (411–6389)	8530 (1431–20 308)	931 (338–3521)	<.001
	Rehabilitation	2661 (0–25 481)	12 363 (971–27 500)	1594 (0–22 497)	.055
Cost of hospital day, 2019 euro, median (IQR) <sup>a</sup>		1578 (1080–2519)	1367 (877–2863)	1604 (1094–2499)	.805

Abbreviations: IQR, Interquartile range; mRS, modified Rankin Scale; TISS, Therapeutic Intervention Scoring System; APACHE, Acute Physiology and Chronic Health Evaluation; SAPS, Simplified Acute Physiology Score; SOFA, Sequential Organ Failure Assessment.

<sup>a</sup>N=150.

<sup>b</sup>N=139.

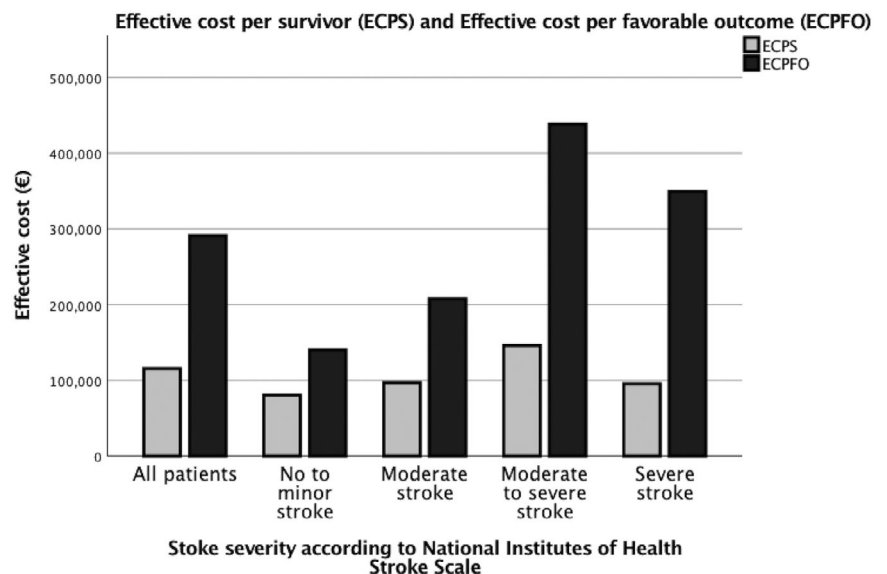


FIGURE 2 Change in ECPS and ECPFO according to stroke severity

TABLE 4 Variables associated with costs of patient care, presented as cost ratios

Variable	Univariate all patients (N = 152)			Univariate hospital survivors (N = 99)		
	Cost ratio	95% CI	p-value	Cost ratio	95% CI	p-value
Age	0.98	0.96–0.99	.002	0.97	0.96–0.99	.001
Max TISS Score	1.05	1.03–1.08	<.001	1.04	1.02–1.07	.001
APACHE II Score	0.96	0.94–0.99	.005	0.99	0.96–1.02	.528
SAPS Score	0.98	0.97–0.99	.004	1.00	0.98–1.01	.550
SOFA Score	1.00	0.94–1.06	.947	1.05	0.99–1.12	.114
Location of Infarct						
Supratentorial	Reference			Reference		
Infratentorial or both	1.24	0.83–1.85	.285	0.99	0.66–1.49	.954
NIHSS	0.99	0.97–1.01	.460	1.01	0.99–1.03	.338
Length of Hospital Stay	1.15	1.09–1.21	<.001	1.02	1.01–1.04	.007
Length of Intensive Care Unit Stay	1.05	1.04–1.06	<.001	1.08	1.03–1.13	.001
WHO/ECOG performance status						
Fit for work	Reference			Reference		
Independent in self-care	0.55	0.30–1.03	.060	0.59	0.31–1.10	.096
Partially dependent	0.97	0.48–1.96	.925	0.65	0.35–1.23	.181
Multivariate all patients (N = 152)						
Age	0.99	0.98–1.00	.150	Multivariate hospital survivors (N = 99)		
Max TISS Score	1.02	1.00–1.05	.088	0.98	0.97–0.99	.004
APACHE II Score	0.99	0.95–1.03	.627	Excluded from analysis		
SAPS Score	1.00	0.98–1.02	.710	Excluded from analysis		
Length of Hospital Stay	1.04	1.03–1.05	<.001	1.01	1.00–1.03	.407
Length of Intensive Care Unit Stay	1.05	0.99–1.11	.090	1.02	0.97–1.08	.100
$R^2$ 0.367			$R^2$ 0.236			
F-test 14.006			F-test 7.279			
VIF-max 3.84			VIF-max 1.54			

Abbreviations: CI, confidence interval; TISS, Therapeutic Intervention Scoring System; APACHE, Acute Physiology and Chronic Health Evaluation; SAPS, Simplified Acute Physiology Score; SOFA, Sequential Organ Failure Assessment; NIHSS, National Institutes of Health Stroke Scale; WHO/ECOG, World Health Organization/Eastern Cooperative Oncology Group.

## 4.2 | Relationship with previous studies

In Europe, the annual expenditure of stroke has been estimated at 27 billion euros, where approximately two-thirds comprise direct medical expenses and one-third is indirect costs.<sup>23,24</sup> Increase in age, prolonged patient survival, poor neurological outcomes, and prolonged LOS at hospital have been reported to increase costs.<sup>14,25–27</sup> Prior to this study, reports on the long-term prognosis, and resource use of AIS patients admitted to ICU care have been lacking. However, we have reported 1-year mean costs per patient at 39,222€, ECPS at 55,543€, and effective cost per independent survivor at 104,734€ (2013 euro) in an earlier multi-center study.<sup>15</sup> In the current single-center study, total costs were markedly higher, likely due to the patients being more critically ill as compared with APACHE II and SAPS scores (median scores being 24 vs 14 and 53 vs 29, respectively). This is likely due to the studied hospital being the regional referral

center for patients needing thrombolysis or thrombectomy, concentrating critically ill patients to the hospital.

This study has shown that post-ICU costs are high and that cost-effectiveness declines with increasing stroke severity and increasing age; indeed, a large proportion of patients are not rehabilitated enough to gain independence. In the severe stroke group, the cost-effectivity increased somewhat compared with the moderate to severe group, most likely due to a more stringent reflection on admittance to the ICU, as these patients are prone to being seen as “beyond recovery” by the admitting clinician. On the other hand, the prognosis of patients in the moderate to severe stroke group is often uncertain, and thus admittance to the ICU can readily be justified.

As reported in earlier studies, LOS at hospital was an independent predicting factor for costs. Contrary to earlier reports, our study shows that an increase in age at incident actually decreased



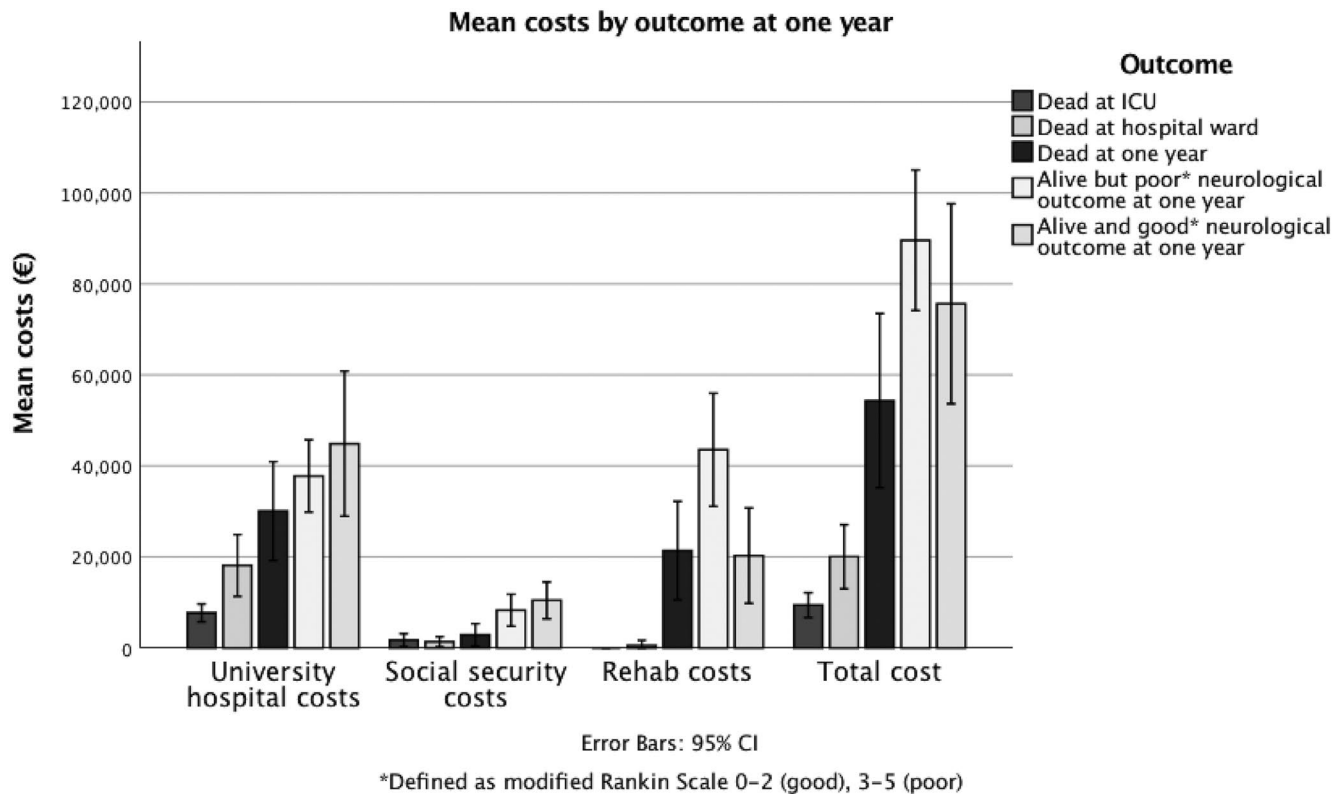


FIGURE 3 Bar-chart describing mean costs at 1 year, grouped according to outcome

the costs for hospital survivors. A possible explanation for this is that although high age is not regarded as a reason not to admit a patient to the ICU, the clinician making admissions might be biased to admit younger patients more easily compared with an elderly patient with the same pre-admission performance status and stroke severity, i.e. ICU-admitted older patients are relatively more healthy than younger patients. The observed cost of care for older patients seems lower, as only those with a good outcome potential would be selected to receive more aggressive treatment. Older patients also generally survive a shorter time in critical care and thus accumulate costs for a shorter time.

A supratentorial location of the ischemic lesion was associated with a reduced OR. These patients often had a middle cerebral artery infarction ("malignant MCA infarction"), anterior cerebral artery infarction, or multiple ischemic lesions and thus a large affected area of the brain, explaining their low odds of recovery.

During the study period, MT was not yet in routine use, and thus only a few patients in the studied population underwent the procedure. Our conjecture is that since the study period, the routine use of MT could have increased the number of patients needing ICU-level care due to more need for sedation and mechanical ventilation and organ support. By increasing the portion of favorable neurological outcomes, this could reduce the final ECPFO. This idea is however contested by the findings in a recent mail study of ICUs in Europe and worldwide, which showed that according to estimates made by neurointensivists, less than 10 percent of AIS patients cared for in

ICUs are admitted after MT. In addition, the impression of the surveyed neurointensivists was that ICU-resources are mainly used for the sicker AIS patients who require more advanced care than simple post MT monitoring.<sup>28</sup> On the other hand, increased use of MT could also reduce the number of patients needing ICU-level care in the first place by reducing the number of severe (e.g. malignant MCA) strokes.

### 4.3 | Strengths and limitations

We note some strengths with the current study. Conducted in a country with a government-funded security system covering costs of medical care, we were able to calculate true medical costs. Social security also reimburses the costs of private doctors and physiotherapy, medicine, and medical transport, and these expenses are well recorded. In addition, our study included prospective data collection on treatment intensity in the ICU.

However, we note some limitations. Firstly, the cohort studied is from the era before MT was in routine use, and we cannot exclude other possible changes in ICU-care since or during the studied time-period, leading to changes in the costs of care. Thus the population may not fully represent the patient selection cared for in present-day ICUs and the costs may not adequately represent the current expenses in ICU-care. Secondly, patient medical records were used to assess most of the NIHSS and mRS

retrospectively. These were nonetheless performed by a senior house officer in neurology with relevant experience. Thirdly, the indication for ICU admittance was estimated on the basis of patient journal notes and, as only one indication was allowed for, the groups can hide the complexity of the clinical situation. Therefore, we declined to do a more granular analysis of the material, as we feared this could lead to oversimplification of a complex situation. Lastly, the studied population was small; thus, our findings need validation in larger samples.

## 5 | CONCLUSION

In this study focusing on care of AIS patients between 2003 and 2013, an era predating MT, we found ICU care is often costly and that the outcomes are often poor, especially in patients with more severe disease and higher age. Further studies focusing on more recent years are needed to better target ICU care and identify cases with a low likelihood of good long-term outcomes.

### CONFLICTS OF INTEREST

Markus B Skrifvars reports lecture fees and travel grants from BARD Medical (Ireland).

All other authors report that they have no conflicts of interest.

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### REFERENCES

- Johnson CO, Nguyen M, Roth GA, et al. Global, regional, and national burden of stroke, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet Neurol.* 2019;18(5):439–458. doi:10.1016/S1474-4422(19)30034-1
- Vos T, Lim SS, Abbafati C, et al. Global burden of 369 diseases and injuries in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet.* 2020;396(10258):1204–1222. doi:10.1016/S0140-6736(20)30925-9
- Krishnamurthi RV, Barker-Collo S, Parag V, et al. Stroke incidence by major pathological type and ischemic subtypes in the Auckland Regional Community Stroke Studies: changes between 2002 and 2011. *Stroke.* 2018;49(1):3–10. doi:10.1161/STROKEAHA.117.019358
- Zazulia AR. Critical care management of acute ischemic stroke. *Contin Lifelong Learn Neurol.* 2009;15:68–82. doi:10.1212/01.CON.0000348810.14427.c5
- Kirkman MA, Citerio G, Smith M. The intensive care management of acute ischemic stroke: an overview. *Intensive Care Med.* 2014;40(5):640–653. doi:10.1007/s00134-014-3266-z
- Meyfroidt G, Bollaert P-E, Marik PE. Acute ischemic stroke in the ICU: to admit or not to admit? *Intensive Care Med.* 2014;40(5):749–751. doi:10.1007/s00134-014-3289-5
- Navarrete-Navarro P, Rivera-Fernández R, López-Mutuberría MT, et al. Outcome prediction in terms of functional disability and mortality at 1 year among ICU-admitted severe stroke patients: a prospective epidemiological study in the south of the European Union (Evascan Project, Andalusia, Spain). *Intensive Care Med.* 2003;29(8):1237–1244. doi:10.1007/s00134-003-1755-6
- Golestanian E, Liou JI, Smith MA. Long-term survival in older critically ill patients with acute ischemic stroke. *Crit Care Med.* 2009;37(12):3107–3113. doi:10.1097/CCM.0b013e3181b079b2
- Rordorf G, Koroshetz W, Efirid JT, Cramer SC. Predictors of mortality in stroke patients admitted to an intensive care unit. *Crit Care Med.* 2000;28(5):1301–1305.
- Broessner G, Helbok R, Lackner P, et al. Survival and long-term functional outcome in 1,155 consecutive neurocritical care patients. *Crit Care Med.* 2007;35(9):2025–2030. doi:10.1097/01.ccm.0000281449.07719.2b
- Riachy M, Sfeir F, Sleilaty G, et al. Prediction of the survival and functional ability of severe stroke patients after ICU therapeutic intervention. *BMC Neurol.* 2008;8(1):24. doi:10.1186/1471-2377-8-24
- Kipthuth IC, Schellinger PD, Köhrmann M, et al. Predictors for good functional outcome after neurocritical care. *Crit Care.* 2010;14(4):R136. doi:10.1186/cc9192
- Alonso A, Ebert AD, Kern R, Rapp S, Hennerici MG, Fatar M. Outcome predictors of acute stroke patients in need of intensive care treatment. *Cerebrovasc Dis.* 2015;40(1–2):10–17. doi:10.1159/000430871
- Meretoja A, Kaste M, Roine RO, et al. Direct costs of patients with stroke can be continuously monitored on a national level: performance, effectiveness, and costs of treatment episodes in Stroke (PERFECT Stroke) Database in Finland. *Stroke.* 2011;42(7):2007–2012. doi:10.1161/STROKEAHA.110.612119
- Raj R, Bendel S, Reinikainen M, et al. Costs, outcome and cost-effectiveness of neurocritical care: a multi-center observational study. *Crit Care.* 2018;22(1):225. doi:10.1186/s13054-018-2151-5
- Pekkarinen PT, Bäcklund M, Efendijev I, et al. Association of extracerebral organ failure with 1-year survival and healthcare-associated costs after cardiac arrest: an observational database study. *Crit Care.* 2019;23(1): doi:10.1186/s13054-019-2359-Z
- Brott T, Adams HP, Olinger CP, et al. Measurements of acute cerebral infarction: a clinical examination scale. *Stroke.* 1989;20(7):864–870. doi:10.1161/01.STR.20.7.864
- Williams LS, Yilmaz EY, Lopez-Yunez AM. Retrospective assessment of initial stroke severity with the NIH Stroke Scale. *Stroke.* 2000;31(4):858–862. doi:10.1161/01.STR.31.4.858
- Tilastokeskus - Statistics Finland. Suomen virallinen tilasto (SVT): Kuluttajahintaindeksi [verkkójulkaisu]. <https://www.tilastokeskus.fi/tup/laskurit/rahanarvonmuunnin.html>. Accessed August 6, 2020.
- Meretoja A, Strbian D, Mustanoja S, Tatlisumak T, Lindsberg PJ, Kaste M. Reducing in-hospital delay to 20 minutes in stroke thrombolysis. *Neurology.* 2012;79(4):306–313. doi:10.1212/WNL.0B013E31825D6011
- PERFECT - Stroke: Hoitoketjujen toimivuus, vaikuttavuus ja kustannukset aivoverenkiertohäiriöpotilailla. <https://www.julkari.fi/handle/10024/75720> Accessed November 2, 2021
- Jc G. Fifty years of acute ischemic stroke treatment: a personal history. *Cerebrovasc Dis.* 2021;50(6):666–680. doi:10.1159/000519843
- Rajsic S, Gothe H, Borba HH, et al. Economic burden of stroke: a systematic review on post-stroke care. *Eur J Heal Econ.* 2019;20(1):107–134. doi:10.1007/s10198-018-0984-0
- Luengo-Fernandez R, Gray AM, Rothwell PM. Costs of stroke using patient-level data: a critical review of the literature. *Stroke.* 2009;40(2):e18–23. doi:10.1161/STROKEAHA.108.529776
- Dawson J, Lees JS, Chang T-P, et al. Association between disability measures and healthcare costs after initial treatment for

- acute stroke. *Stroke*. 2007;38(6):1893-1898. doi:10.1161/STROKEAHA.106.472381
26. Lekander I, Willers C, von Euler M, et al. Relationship between functional disability and costs one and two years post stroke. *PLoS One*. 2017;12(4):e0174861. doi:10.1371/journal.pone.0174861
  27. Jørgensen HS, Nakayama H, Raaschou HO, Olsen TS. Acute stroke care and rehabilitation: an analysis of the direct cost and its clinical and social determinants. *Stroke*. 1997;28(6):1138-1141. doi:10.1161/01.STR.28.6.1138
  28. Robba C, Giovannini M, Meyfroidt G, et al. Intensive care admission and management of patients with acute ischemic stroke: a cross-sectional survey of the European Society of Intensive Care Medicine. *J Neurosurg Anesthesiol*. 2021; Publish Ahead of Print. doi:10.1097/ANA.0000000000000761

## SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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