The Evaluation of the Stroke Unit in Croatia at the University Hospital »Sestre milosrdnice«, Zagreb: 1995–2006 Experience

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A B S T R A C T

This study evaluate the effects of the Stroke Unit (SU) in Croatia by comparing the in-hospital case fatality rate in the period before (1995–2000) and after (2001–2006) the implementation of SU and to compare the prevalence of risk factors, such as hypertension, diabetes mellitus (DM), atrial fibrillation (AF) and ischemic heart disease (IHD) among the patients who died. The study was conducted in twelve-year period during which 10 901 stroke patients were admitted to hospital and 1 818 of them died. The endpoints were in-hospital case fatality rate and prevalence of risk factors among the patients who died. Before the SU period the case fatality rate was 20.1%, whereas afterwards it decreased significantly to 12.8% (p<0.001). The relative risk (RR) was 1.57, while the estimate of the odds ratio (OR) showed a 71% increase in chances of death in the pre-SU period. The prevalence of DM, IHD and AF increased significantly, while hypertension was the only risk factor which significantly decreased (p<0.001). The results showed that the implementation of SU care is associated with a significant reduction of in-hospital case fatality rate of acute stroke patients which strongly suggests that development of the SU network in Croatia should be given priority in the health management.

Key words: *stroke mortality, stroke unit, Croatia, in-hospital case fatality*

Introduction

Stroke is a worldwide health problem marked with high morbidity, mortality, disability and high health care costs. In Croatia it is the second specific cause of death for both genders[1]. According to the WHO recommendations and the European Stroke Initiative, every stroke patient in the acute phase should be treated by a specialized stroke team in a specialized stroke unit. The concept of organized care on geographically-defined units has given rise to a more disease-specific approach to the management of stroke[2,3].

Treatment of stroke patients in SU improves the outcome compared with treatment in general wards by reducing mortality, institutionalization and dependency[4]. The reduction in the risk of death after a stroke is achieved through prevention and treatment of secondary complications, in particular of infections[5]. Most studies compared the outcome of stroke patients admitted to stroke units with patients hospitalized in general medical or geriatric wards, but only few studies included patients hospitalized in a neurology ward as the control group[5,6].

The SU have been founded in the end of the 20th century in some USA university hospitals and in Croatia such intensive care for stroke patients was founded in Rebro Hospital in 1971. At the University Hospital »Sestre milosrdnice« in Zagreb, the Stroke Unit in Croatia was implemented at the beginning of the year 2001 as a hospital ward with 10 beds and a dedicated multidisciplinary stroke team consisting of neurologists specialized in the management of cerebrovascular diseases, trained nurses, and employees who participate in the rehabilitation care, such as a physiotherapist and a speech and lan-

guage therapist. Before this specialized unit was established stroke patients were treated at the conventional neurological ward together with patients suffering from other neurological illness.

The purpose of this study was to examine the effects of the stroke unit care for stroke patients by comparing the in-hospital case fatality rate in the period before (1995–2000) and after (2001–2006) the implementation of stroke unit. Since a considerable number of stroke patients who died had hypertension, diabetes mellitus (DM), atrial fibrillation (AF) and ischemic heart disease (IHD), we also compared the prevalence of these risk factors and co-morbidity in the above mentioned periods.

Patients and Methods

This is a retrospective study of acute stroke in-patients conducted between the 1st of January, 1995 and the 31st of December, 2006 at the University Hospital »Sestre milosrdnice«, Department of Neurology, Zagreb.

In the above mentioned period 10 901 patients with symptoms of acute stroke were admitted to general emergency rooms and subsequently hospitalized at the Department of Neurology and the Stroke Unit. A total of 1 818 stroke patients died, 794 male and 1 024 female. In the assessment of the stroke we used established diagnostic criteria and all patients went through detailed neurological and general physical examination[2]. Data were collected from the medical records of the stroke in-patients stored in the hospital-based registry. Patients with ischemic and hemorrhagic strokes were included into the study, while patients with subarachnoid hemorrhage, transient ischemic attacks and those with the clinical presentation of stroke two weeks before hospitalization were excluded from the study.

Statistical analysis

To describe and to estimate the difference between in-hospital case fatality rate and the prevalence of major risk factors and co morbidity in the period before (1995–2000) and after (2001–2006) the implementation of the stroke unit, we used descriptive statistics, the t-test for proportions, the risk ratio and the odds ratio. Additionally, in order to test differences between proportions we performed the Fisher Exact Test when values were smaller than 5 in the 2x2 contingency table. The level of significance was chosen at p<0.001 and the results were shown with 95% confidence intervals (CI). A statistical analysis was performed with the Statistical Package for Social Sciences 14.0 for Windows (SPSS Inc., Chicago, IL, USA).

Results

In the 1995–2006 period, a total of 10 901 stroke patients were admitted to the conventional neurological department and in the stroke unit; 5 730 in the 1995–2000 period and 5 171 in the 2001–2006 period. In the above

mentioned periods a total of 1 818 stroke patients died, 794 male (43.7%) and 1, 024 (56.3%) female. In the 1995–2000 period 1 154 stroke patients died, the number of male and female patients who died were 506 and 648, and in the 2000–2006 period 664 patients died, 288 men and 376 women (Figure 1).

Age range of patients who died was between 25 and 102 years of age. The mean age for males and females for all analyzed years was higher than 70 years of age (Figure 2).

The mean age for all patients was 73.92 (SD=11.38) years, for male patients it was 71.49 (SD=11.858) years and for female patients 75.8 (SD=10.549) (data not shown). The peak occurrence of stroke-related death for male patients was at the age of 71 years, while for female patients there were two peaks, at the age of 79 and 81 (Figure 3).

After the implementation of the stroke unit there was a significant reduction in the in-hospital case fatality rate (t (10832)=10.35; p<0.001). Before the stroke unit was implemented the case fatality rate was 20.1% (SD=0.40), while after that period it decreased to 12.8% (SD=0.34). The difference between proportions was 7.3% (SD=0.73, 95% CI: 0.0592, 0.0868). The Fisher Exact Test was also significant p<0.001. The risk ratio was 1.57 (95% CI: 1.4366, 1.7123) while the odds ratio was 1.71 (95% CI: 1.5427, 1.8993) (Figure 4).

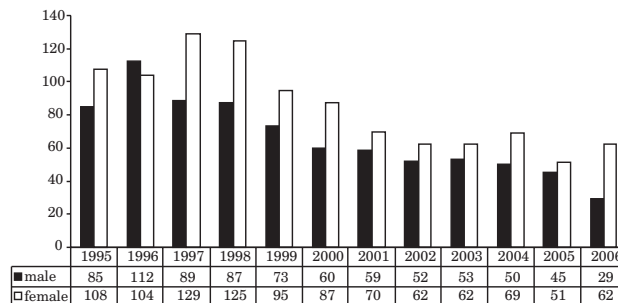|	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006
■ male	85	112	89	87	73	60	59	52	53	50	45	29
□ female	108	104	129	125	95	87	70	62	62	69	51	62

Fig. 1. Distribution of the acute stroke patients who died in the 1995–2000 and 2001–2006 periods according to gender.
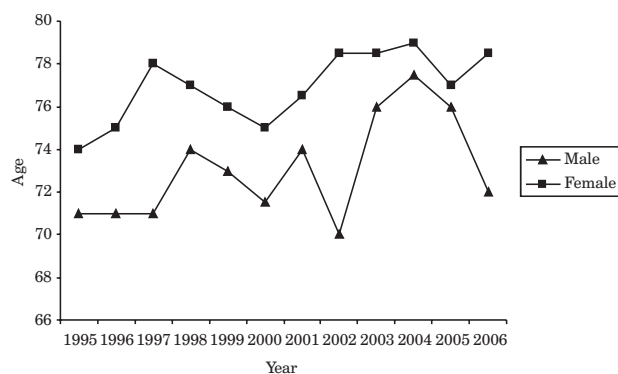

Fig. 2. The mean age of stroke patients who died in the 1995–2000 and 2001–2006 periods according to gender.
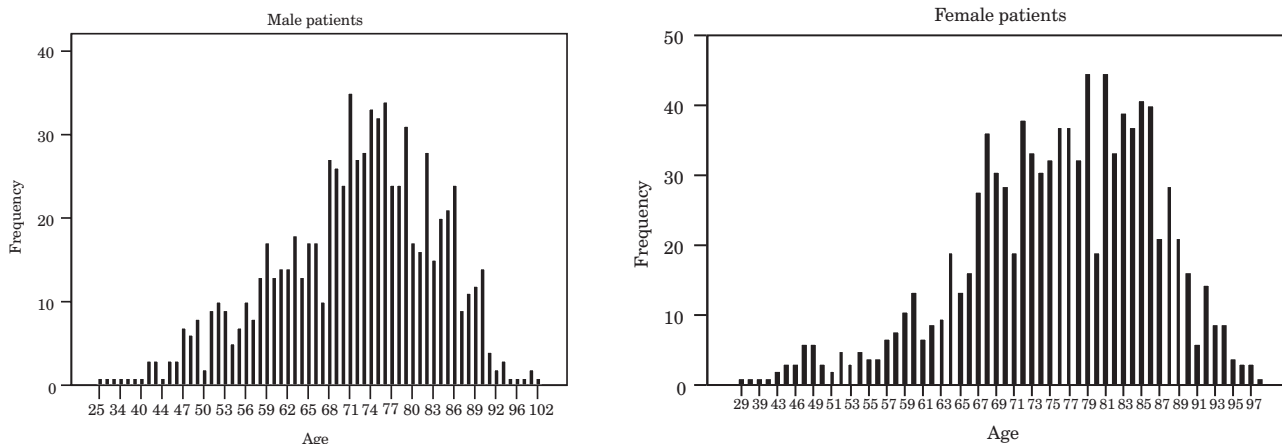
Fig. 3. The peak occurrence of stroke-related death for male and female patients.

Comparison of prevalence of hypertension, DM, AF, and IHD among stroke patients who died in the 1995––2000 and 2001–2006 periods

After the implementation of the stroke unit the proportion of patients with hypertension who died significantly decreased $t(1293)=2.15$; $p=0.032$. The difference between proportions was 4.2% (SD=0.71, 95% CI: 0.0038, 0.0807). Before the stroke unit was implemented the proportion of hypertension was 82.2% (SD=0.38), whereas after the implementation of the stroke unit it decreased to 78% (SD=0.41). The risk ratio was 1.05 (95% CI: 1.0043, 1.1065), while the odds ratio was 1.31 (95% CI: 1.0287, 1.6549).

After the implementation of the stroke unit the proportion of patients with diabetes mellitus who died significantly increased $t(1276)=3.21$; $p=0.001$. In the period before the implementation of the stroke unit this proportion was 20.8% (SD=0.41), whereas after this period it increased up to 27.6% (SD=0.45). The risk ratio was 0.75 (95% CI: 0.6386, 0.8918), which means that the proportion of patients with DM who died was 25% lower before the stroke unit was implemented, while the odds ratio was 0.69 (95% CI: 0.5529, 0.8615).

After the implementation of the stroke unit the proportion of stroke patients with ischemic heart diseases who died increased significantly $t(1245)=2.48$; $p=0.013$. The difference between proportions was 4.3% (SD=0.61, 95% CI: 0.0767, 0.0089). Before the stroke unit was implemented the proportion of IHD was 12.1% (SD=0.33), whereas afterwards it increased to 16.4% (SD=0.37). The risk ratio was 0.74 (95% CI: 0.5863, 0.9315) which means that the proportion of IHD among the patients who died was 26% lower before the implementation of the stroke unit while the odds ratio was 0.70 (95% CI: 0.5362, 0.9217).

Our data show that after the implementation of the stroke unit the proportion of stroke patients with atrial fibrillation who died increased significantly $t(1233)=4.60$; $p<0.001$. The difference between proportions was 9.7% (SD=0.74, 95% CI: 0.1387, 0.0557). Before the implementation of the stroke unit the proportion of AF was 19.5% (SD=0.40), whereas after that period the proportion increased to 29.2% (SD=0.46). The risk ratio was 0.67 (95% CI: 0.5649, 0.7883), which means that the proportion of AF was 33% lower in the period before the stroke unit, while the odds ratio was 0.59 (95% CI: 0.4701, 0.7325).
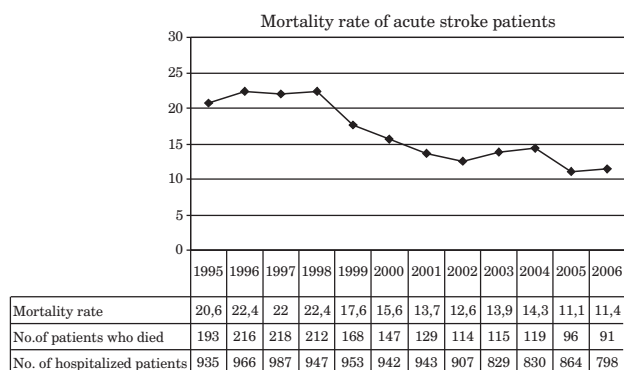
Discussion

In our study we confirmed that the implementation of the Stroke Unit at the Department of Neurology in the University Hospital »Sestre milosrdnice« in Zagreb is associated with a significant reduction of the in-hospital case fatality rate of acute stroke patients.

Such results were not unexpected since several studies proved that the Stroke Units' care improves the outcome of stroke patients. The superiority of the Stroke Unit to the general rehabilitation unit is widely accepted. A meta-analysis conducted by the Stroke Unit Trialists' Collaboration showed a reduction in the case fatality rate up to 25% for patients treated in a Stroke Unit in comparison with patients in a general medical ward, as well

	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006
Mortality rate	20,6	22,4	22	22,4	17,6	15,6	13,7	12,6	13,9	14,3	11,1	11,4
No. of patients who died	193	216	218	212	168	147	129	114	115	119	96	91
No. of hospitalized patients	935	966	987	947	953	942	943	907	829	830	864	798

Fig. 4. Mortality rate in the 1995–2000 and the 2001–2006 periods.

as a reduction in dependence and the need for institutional care[4]. On the other hand, the number of studies that compare the effectiveness of treatment in a SU with a treatment in a general neurological ward is limited. Krespi et al. showed in their study a significantly lower in-hospital case fatality in the SU, 10.5% *vs*. 19.6% at the general neurological ward[7].

This study was not designed to detect which component in the medical care mostly contributed to the reduction of death among the acute stroke patients, but this effect can be explained with a combination of essential components of an organized acute stroke care such as: early medical assessment and diagnosis including computerized tomography scanning; early assessment of nursing and therapy needs; early mobilization, prevention of complications and treatment of hypoxia, hyperglycemia, pyrexia and dehydration and finally, implementation of early rehabilitation policies in coordinated multidisciplinary team care with assessment of needs after discharge[8,9]. The most recent review published by Govan et al. included data from 17 trials with 3 327 participants. They grouped complications as physiological, neurological, cardiovascular, complications of immobility, and others, and confirmed that the stroke units care reduced case fatality, particularly deaths attributed to complications of immobility (OR=0.59; CI:0.41 to 0.86). Such care was also associated with statistically significant increases in the reported use of oxygen and paracetamol, and measures to prevent aspiration, while the reduction of the use of urinary catheterization was non significant. The statistically significant reduction in the stroke progression/recurrence was observed (OR=0.66, CI: 0.46 to 0.95) as well in some complications of immobility, such as chest and other infections and pressure sores, while there were no significant differences in the cardiovascular, physiological, or other complications[5].

Among the 1,818 stroke patients who died in the investigated period the proportion of females was, as we expected, higher that the proportion of males, 794 male patients (43.7%) *vs*. 1,024 (56.3%) female patients. This ratio was kept for all investigated years with the single exception of the year 1996. In the 1995–2000 period the numbers of men and women who died were 506 and 648, and in the 2001–2006 period 288 and 376, respectively. Age range of patients who died in the selected 12-year period was wide, starting from 25 to 102 years of age. The peak occurrence of stroke-related death for male patients was at the age of 71 years and for female patients at the age of 79 and 81 years. The majority of stroke patients who were hospitalized and died at the conventional neurological department and the SU were older than 65 years of age. The treatment of these patients is challenging since they have many chronic diseases, such as hypertension and diabetes mellitus, which increases the in-hospital mortality, complications and the health care costs. According to our study, the prevalence of diabetes mellitus, ischemic heart diseases and atrial fibrillation increased significantly among the patients who died, while hypertension was the only one which decreased

significantly in the investigated period. These findings are useful for the future clinical guidelines of a multidisciplinary stroke team but attention is needed with any further interpretation of these findings since the source population is limited to one area in the City of Zagreb and it is hardly representative of the Croatian population in general.

According to the data from the »European Health for All Database« in the year 1991 the standardized death rate (SDR) of cerebrovascular diseases per 100,000 inhabitants of all ages in Croatia was 165.91 and it grew constantly until the year 1998 when it reached its peak – 188.18. In the year 2005 the SDR for cerebrovascular diseases was 131.83/100 000. Despite the recent decrease in the mortality, this rate is still higher than rates in other transitional countries such as Hungary (108.23/100,000), Slovakia (74.22/100 000), and Slovenia (63.0/100,000) and almost double than the EU average – 69.4/100 000[10,11].

Polic-Vizintin et al. conducted a survey in the City of Zagreb, which comprises of the majority of the Croatian population, and which showed a constant rise of circulatory diseases as a cause of death in the 30-year period (1971–2001)[12]. This trend in the capital unfortunately represents a rule rather than an exception and similar trends are also observed in the majority of Croatian regions. The burden of complex diseases in Croatia shows strong geographical variation with a several fold differences in morbidity and mortality among coastal and continental parts of the country. Still, although mortality trends of cerebrovascular diseases stagnated or even declined in the Mediterranean region, the secular trend for the entire country shows a constant rise[13]. During the war in Croatia (1991–1995) the incidence of stroke increased not only in the Eastern Croatia but also in the Dalmatian region[14,15].

Despite the limitations, this study that evaluates the effect of the stroke units' care for acute stroke patients in Croatia and emphasizes the need for implementation of more of such units. Croatia is still facing a dynamic transitional process accompanied with well-known socio-economic changes that affect all aspects of life. SDRs for some complex diseases exceed those reported in neighboring countries and an increase in the cardiovascular death rates can largely be explained with high prevalence of major risk factors, such as smoking and hypertension[16]. To decrease the burden of chronic diseases modification of unhealthy behavior in the population such as smoking, physical inactivity, and dietary issues through the implementation of preventive programs is essential. Besides the most efficient primary prevention, the future health policies should also include adequate numbers of beds in specialized stroke units. These aims were so far hard to reach mostly because of the lack of understanding and limited resources. It is often pointed out that the stroke units' care is proven to be beneficial but costly, although such treatment tends to decrease post-acute in-patient care costs. Compared to patients a general ward, the SU stroke patients were able to return to their normal daily activities earlier, they have better social abili-

ties and reduced neurological defects, without increasing the overall economic burden[17]. Until now the cost-efficiency analysis for acute stroke care was not conducted in Croatia, but according to such analysis in other countries the differences in the costs are not as high as hard critics would think. The similar research in Germany showed that acute stroke unit care is approximately 16% more costly than treatment on regular neurological wards due to higher resource use of personnel and diagnostic procedures[18]. The population aging emphasizes the increasing importance of non-communicable diseases and by the year 2020, the stroke and other cardiovascular diseases will be the leading causes of lost healthy life-years[19]. Some transitional countries, such as Poland, prepared to meet future needs and demands and already evaluated the accessibility of their stroke units and dynamically developed the stroke unit network[20].

Croatia is not spared from the population aging and mortality of selected non-communicable, chronic diseases is predicted to increase in the future and remain relatively high. The result of a 71% reduction in-hospital case fatality rate in SU at Department of Neurology, University Hospital »Sestre milosrdnice« is important to underline the necessity to introduce more SU in Zagreb and whole Croatia. The significant reduction in the fatality rate of acute stroke patients, observed in the study, strongly suggests that the development of the SU network in Croatia should be given priority in health sevice organization. The outcome of this research should emphasize the urgent need for prioritizing the stroke prevention and management in the future health management and policy.

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PROCJENA UČINKOVITOSTI JEDINICE ZA LIJEČENJE MOŽDANOG UDARA NA KLINICI ZA NEUROLOGIJU KB »SESTRE MILOSRDNICE«, ZAGREB, HRVATSKA, U RAZDOBLJU OD 1995. DO 2006. GODINE

SAŽETAK

Prikazani su rezultati procjene učinkovitosti Jedinice za liječenje moždanog udara (JLMU) na Klinici za neurologiju KB »Sestre milosrdnice« uspoređivanjem bolničkog mortaliteta u periodu prije (1995.–2000.) i poslije (2001.–2006.) njezinog uvođenja. Učinjena je i usporedba rizičnih čimbenika za nastanak bolesti, kao što su primjerice hipertenzija, šećerna bolest, atrijska fibrilacija i ishemična bolest srca, u populaciji preminulih bolesnika. Istraživanje je provedeno u dvanaestogodišnjem razdoblju tijekom kojeg je hospitalizirano 10,901 bolesnika s akutnim moždanim udarom, a preminulih je bilo 1,818. Uspoređivanjem mortaliteta bolesnika s akutnim moždanim udarom tijekom bolničkog liječenja i prevalencije rizičnih faktora među preminulim bolesnicima utvrđeno je da je prije uspostavljanja JLMU-a taj mortalitet iznosio je 20,1%, dok se nakon njezinog utemeljenja statistički značajno snizio na 12,8% (p<0,001). Relativni rizik (RR) bio je 1,57, dok je procjena omjera šansi (engl. odds ratio, OR) pokazala 71%-tno povećanje šansi smrtnog ishoda u

razdoblju prije osnivanja JLMU-a. Prevalencija šećerne bolesti, ishemične srčane bolesti i atrijske fibrilacije značajno je porasla u istraživanoj populaciji, dok je hipertenzija jedini rizični čimbenik koji bilježi statistički značajno smanjenje učestalosti (p<0,001). Ovim istraživanjem potvrdili smo da je organizacija i uspostavljanje JLMU-a povezana s značajnim smanjenjem mortaliteta tijekom bolničkog liječenja bolesnika s akutnim moždanim udarom. Rezultati upućuju na potrebu razvoja i uspostavljanja mreže JLMU-a u Hrvatskoj čemu bi se trebao dati prioritet u budućoj organizaciji zdravstvene zaštite.