



A National Survey of Acute Cerebrovascular Disease in Israel: Burden, Management, Outcome and Adherence to Guidelines

David Tanne MD^{1,4}, Uri Goldbourt PhD⁴, Silvia Koton PhD^{2,4}, Ehud Grossman MD^{3,4}, Nira Koren-Morag PhD⁴, Manfred S. Green MD PhD^{2,4} and Natan M. Bornstein MD^{1,4} on behalf of the National Acute Stroke Israeli Survey Group*

¹ Israel Neurological Association

² Israel Center for Disease Control (ICDC), Ministry of Health, Tel Hashomer, Israel

³ Israel Society of Internal Medicine

⁴ Sackler Faculty of Medicine, Tel Aviv University, Ramat Aviv, Israel

Key words: stroke, national registry, outcome

Abstract

Background: There are no national data on the burden and management of acute cerebrovascular disease in Israel.

Objectives: To delineate the burden, characteristics, management and outcomes of hospitalized patients with acute cerebrovascular disease in Israel, and to examine adherence to current guidelines.

Methods: We prospectively performed a national survey in all 28 hospitals in Israel admitting patients with acute cerebrovascular events (stroke or transient ischemic attacks) during February and March 2004.

Results: During the survey period 2,174 patients were admitted with acute cerebrovascular disease (mean age 71 ± 13 years, 47% women; 89% ischemic stroke or TIA, 7% intracerebral hemorrhage and 4% undetermined stroke). Sixty-two percent of patients were admitted to departments of medicine and a third to neurology, of which only 7% were admitted to departments with a designated stroke unit. Head computed tomography was performed during hospitalization in 93% of patients. The overall rate of urgent thrombolytic therapy for acute ischemic stroke was 0.5%. Among patients with ischemic stroke or TIA, 94% were prescribed an antithrombotic medication at hospital discharge, and among those with atrial fibrillation about half were prescribed warfarin. Carotid duplex was performed in 30% and any vascular imaging study in 36% of patients with ischemic events. The mean (\pm SD) length of hospital stay was 12 ± 27 days for ICH and 8 ± 11 days for ischemic stroke. Among patients with ICH, 28% died during hospitalization and 66% died or remained with severe disability while for ischemic stroke the corresponding rates were 7% and 41% respectively. Mortality rates within 3 months were 34% for ICH and 14% for ischemic stroke.

Conclusions: This national survey demonstrates the high burden of acute stroke in Israel and reveals discordance between existing guidelines and current practice. The findings highlight important areas for which reorganization is imperative for patients afflicted with acute stroke.

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In Israel, as in the United States and most European countries, stroke is the third most common cause of death [1]. The main burden of stroke, however, is the severe long-term disability associated with it. National data on the burden and management of acute stroke in Israel are lacking. As the management of acute ischemic stroke advances, widespread implementation of optimal stroke care continues to pose enormous challenges for healthcare systems. Clinical guidelines have been developed to provide timely and appropriate decisions for patients admitted with acute stroke [2-5]. We conducted the first survey of all hospitalized patients in Israel with an acute cerebrovascular event during a 2 month period in 2004 to assess the burden of acute cerebrovascular disease, characteristics of patients, management, clinical outcome, and adherence to current practice guidelines.

Patients and Methods

We performed prospectively an observational survey of all consecutive hospitalized patients with acute cerebrovascular disease (stroke or transient ischemic attack) hospitalized in Israel's medical centers during a 2 month period (February to March 2004). The study included all patients with acute stroke or TIA aged 18 or more years, hospitalized in the 28 medical centers in Israel that admit patients with acute stroke. In each hospital a coordinating physician was selected to be responsible for data collection in the hospital departments. Data were collected prospectively. Stroke and TIA were reported in accordance with the medical report on discharge from the hospital. Ischemic stroke and intracerebral hemorrhage were differentiated by findings from head computerized tomography and were regarded as undetermined stroke if brain CT or magnetic resonance imaging were not performed. Cases of subarachnoid hemorrhage and cerebral venous thrombosis were not included in the current survey. Whenever the coordinating physician raised doubt regarding diagnosis, a central adjudication committee made the final decision. A comprehensive questionnaire – including

* See Appendix

TIA = transient ischemic attack

ICH = intracerebral hemorrhage

demographic characteristics, stroke severity, type and subtype, diagnostic tests performed, management and clinical outcome – was designed and completed for all patients.

Neurologic deficits were determined according to the National Institute of Health Stroke Scale score, handicap using the modified Rankin scale, clinical subtypes of ischemic stroke using the Oxfordshire Community Stroke Project classification, and ischemic stroke etiology using the TOAST classification [6]. For uniformity of data collection, study investigators underwent training and received a detailed study manual.

Data entry, editing and analysis were performed at the coordinating center of the Israel Society for the Prevention of Heart Attacks. Data checks for completeness and consistency were based on the discharge medical reports attached to each patient form and on computerized data queries. Data were verified using online checks incorporated into the data entry interface and by batch logical checks applied to the database following the data entry process. The study neurologists resolved all queries at the coordinating center, based on data from discharge summaries. Several indicators of process of care for stroke were evaluated in the survey, based on indicators derived from authoritative guidelines and expert panels [Table 1]. Mortality and survival during the first 90 days post-hospitalization were assessed by means of matching patients' files with national mortality data. The SAS-8 software was used for statistical analysis. Differences in age-adjusted rates were compared using the Cochran-Mantel-Haenszel chi-square test.

Results

During the 2 month survey, 2,174 patients with acute cerebrovascular events were hospitalized in medical centers in Israel. Of these events, 89% (n=1,938) were ischemic cerebrovascular (ischemic stroke n=1,558, 80%, and TIA n=380, 20%); 7% (n=159) were intracerebral hemorrhage; and the remaining 4% (n=78), in which brain imaging was not performed, were regarded as un-

Table 1. Indicators of performance of care for patients with acute cerebrovascular events

Indicators	Percent
Use of head computerized tomography	93%
Admission to a department with a designated acute stroke unit	7%
Arrival by ambulance or mobile ICU	49%
Use of thrombolysis (intravenous or intraarterial) in patients with acute ischemic stroke	0.5%
Use of thrombolysis (intravenous or intraarterial) in patients with ischemic stroke presenting within 6 hours of symptom onset	1%
Use of carotid duplex*	30%
Use of any vascular imaging (carotid duplex, transcranial Doppler, CT or MR or conventional angiography)*	36%
Any antithrombotic at hospital discharge*	94%
Warfarin at hospital discharge among patients with atrial fibrillation*	44%
Warfarin at hospital discharge among patients with atrial fibrillation excluding known malignancy, dementia, bleeding complication, peptic disease or NIHSS >20)*	52%

* Restricted to patients with ischemic stroke or TIA

determined stroke. Women comprised nearly half of the patients (n=1,011, 47%). The mean age of the patients was 71 ± 13 years (men 69 ± 13 vs. women 73 ± 13 years; ICH 73 ± 12, ischemic stroke 71 ± 13, TIA 67 ± 16). Twenty-two percent of patients were under the age of 60.

Baseline characteristics are shown in Table 2. The most frequently reported risk factor was hypertension (overall 75%, age-adjusted rate of 79% for ICH and 75% for ischemic stroke) followed by dyslipidemia (46%) and diabetes mellitus (40%). Over a quarter of the patients had had a prior stroke and 17% had atrial fibrillation. Among patients with ischemic stroke who arrived at the hospital 45% came by ambulance and 5% by mobile intensive care unit, while among those with ICH 60% came by ambulance and 11% by mobile ICU. Over 40% of patients with ischemic stroke and only 12% of patients with ICH arrived by private car or independently. Severe neurologic deficits (NIHSS score ≥11) were found in 23% of patients with ischemic stroke and in 50% of patients with ICH, and mild deficits (NIHSS score ≤5) in 49% of patients with ischemic stroke and in 26% of patients with ICH.

The median time (25%–75%) elapsing from arrival at the emergency department to undergoing head CT, available for 73% of patients, was 2.1 hours (range 1.1–4.1) for patients with ICH and 2.7 (1.5–9.9) for patients with ischemic stroke. Seven percent of patients did not have any brain imaging. The median time interval elapsing from the onset of stroke symptoms to hospital arrival, available for only 53% of patients, was 1.2 hours (range 1.0–3.7) for patients with ICH and 4.1 (1.7–11.9) for patients with ischemic stroke. Twenty-four percent of patients arrived within 3 hours of stroke onset. It should be noted that since data on time elapsing were missing for a substantial proportion of cases, the values presented might be biased.

ICU = intensive care unit

NIHSS = National Institute of Health Stroke Scale

Table 2. Baseline characteristics, mode of transportation and stroke severity

	All (n=2,174) No. (%)	Age adjusted rates (%)			P*
		ICH (n=159)	Ischemic events (n=1938)		
			Ischemic stroke (n=1,558)	TIA (n=380)	
Females	1011 (47%)	57%	55%	47%	0.01
Hypertension	1602 (75%)	79	75	69	0.001
Diabetes	847 (40%)	26	41	36	<0.001
Dyslipidemia	969 (46%)	31	45	51	<0.001
Current smoking	389 (19%)	11	19	17	0.19
Atrial fibrillation	357 (17%)	13	18	13	0.08
Congestive heart failure	257 (12%)	11	13	8	0.01
Peripheral vascular disease	173 (8%)	3	9	8	0.04
Past myocardial infarction	360 (17%)	11	17	13	0.01
Angina	357 (17%)	10	18	15	0.01
CABG/PCI	254 (12%)	9	12	11	0.23
Past stroke	594 (28%)	25	28	21	0.02

* For differences between ICH, ischemic stroke and TIA.

CABG = coronary artery bypass graft, PCI = percutaneous coronary intervention

A third of all patients were admitted to neurology departments, of whom only 7% went to departments with a designated stroke unit. Sixty-two percent of patients were admitted to departments of medicine, 4% to geriatrics and 3% to other department types. Ninety-three percent of patients underwent head CT during hospitalization. Among patients with ischemic stroke, the clinical presentation based on the Oxfordshire classification was total anterior circulation in 10%, partial anterior circulation in 40%, posterior circulation in 23%, lacunar in 21% and unknown in 5%. The overall rate of urgent thrombolytic therapy (intravenous recombinant tissue plasminogen activator or intraarterial thrombolysis) for patients with an acute ischemic stroke was 0.5% overall, and 1% among patients presenting within 6 hours of symptom onset.

Among patients with ischemic events, less than one-third underwent carotid duplex evaluation during hospitalization (age-adjusted rates of 28% for ischemic stroke and 36% for TIA), one-fifth underwent echocardiography and only 2% underwent CT or MR angiography [Table 3]. Only 36% of patients underwent at least one vascular imaging study during hospital admission. Due to the limited in-hospital investigations, the

Table 3. In-hospital use of diagnostic tests and medications at discharge

	All (n=2,174) No. (%)	ICH (n=159)	Age adjusted rates (%)		P*
			Ischemic events (n=1938)		
			Ischemic stroke (n=1,558)	TIA (n=380)	
Use of diagnostic tests					
Head CT**	2018 (93%)	100%	100%	81%	-
Head MRI	35 (2%)	1%	2%	1%	0.16
Carotid duplex	599 (28%)	6%	28%	36%	<0.001
Transcranial Doppler	100 (5%)	0%	5%	4%	0.01
CT or MR angiography	47 (2%)	5%	2%	3%	0.21
Cerebral angiography	25 (1%)	1%	1%	2%	0.45
Transthoracic echocardiography	336 (15%)	7%	17%	17%	0.003
Transesophageal echocardiography	53 (2%)	1%	3%	3%	0.45
Medications at discharge among survivors					
Aspirin	1562 (78%)	5	82	83	<0.001
Clopidogrel	268 (14%)	0	14	16	<0.001
Cardoxin	130 (7%)	0	7	6	0.02
Any antiplatelet	1676 (84%)	5	88	89	<0.001
Coumadin	196 (10%)	2	11	11	0.004
Beta-blocker	621 (37%)	36	36	36	0.99
Diuretics	624 (32%)	27	33	27	0.05
ACE inhibitors	927 (47%)	52	48	40	0.002
Calcium channel blocker	610 (31%)	34	30	31	0.73
Angiotensin receptor blocker	101 (5%)	2	6	5	0.19
Statins	814 (41%)	22	40	46	<0.001
Oral hypoglycemics	561 (29%)	13	30	25	<0.001
Insulin	124 (6%)	5	7	3	0.007

* For differences between ICH, ischemic stroke and TIA.

** ICH and ischemic stroke were differentiated by findings from head CT and were regarded as undetermined stroke if brain imaging was not performed.

ACE = angiotensin-converting enzyme

etiology of ischemic strokes based on the TOAST classification was undetermined in 45% of patients, while the most common determined etiologies were small-vessel occlusive disease in 28%, cardioembolism in 19% and large-vessel atherothrombotic disease in 8%.

An antithrombotic medication was prescribed at discharge in 94% of patients with ischemic events, of whom 89% were prescribed a single or combination of antiplatelets (aspirin 83%, clopidogrel 14% and dipyridamole 7%) and 11% warfarin. About half of the potentially suitable candidates with atrial fibrillation after an ischemic cerebrovascular event received warfarin at hospital discharge. Statins were prescribed for 42% of patients with ischemic events (age-adjusted rates of 40% for ischemic stroke and 46% for TIA). Selected indicators of process of care for acute cerebrovascular events, including admission to stroke units, use of thrombolytic therapy, diagnostic tests and medications are shown in Table 1.

Clinical outcomes

Mean length of hospitalization was 12 ± 27 days for patients with ICH and 8 ± 11 days for those with ischemic stroke [median (25%–75%) of 7 days (range 4–13) and 5 (3–9) days, respectively]. The outcomes of all patients afflicted with acute stroke (excluding TIA) are summarized in Table 4. Forty-three percent of patients with acute stroke had poor outcome at hospital discharge (34% severe handicap and 9% died) and an additional 29% had moderate handicap (mRS 2–3). Among patients with ICH, two-thirds had poor outcome (age-adjusted mortality rate

mRS = modified Rankin scale

Table 4. Outcome of patients with acute stroke: functional status, discharge destination, and mortality

	All (n=1,795)* No. (%)	Age adjusted rates (%)		
		ICH (n=159)	Ischemic stroke (n=1,558)	P
Functional status at end of hospitalization				
Mild handicap (mRS 0–1)	506 (27%)	15%	30%	<0.001
Moderate handicap (mRS 2–3)	503 (29%)	19%	29%	
Severe handicap (mRS 4–5)	592 (34%)	38%	34%	
Deceased	162 (9%)	28%	7%	
Discharge destination				
Home	972 (54%)	27%	56%	<0.001
Rehabilitation facility	491 (27%)	29%	28%	
Nursing facility	120 (7%)	11%	6%	
Other/unknown	48 (3%)	6%	2%	
Deceased	162 (9%)	27%	7%	
Mortality				
7 days	89 (5%)	20%	3%	<0.001
30 days	196 (11%)	30%	9%	
3 months	277 (16%)	34%	14%	

* All patients with acute stroke (ischemic, hemorrhagic and undetermined), excluding TIAs

of 28% and severe handicap of 38%) compared with 41% of patients with ischemic stroke (age-adjusted mortality rates of 7% and severe handicap of 34%). A larger proportion of patients with ICH were released to a nursing facility (11%) than patients with ischemic stroke (6%). Less than a third of patients with both ICH and ischemic stroke were discharged to a rehabilitation facility, while over half of the patients with ischemic stroke and over a quarter of the patients with ICH were discharged home. Age-adjusted mortality rates among patients with ICH were 20% within 1 week, 30% within 30 days, and 34% within 3 months. Among patients with ischemic stroke, mortality rates were 3% after 1 week, 9% after 30 days, and 14% after 3 months.

Discussion

This is the first nationwide survey of acute cerebrovascular disease. It is unique as a comprehensive survey, which includes all patients admitted into the various departments of all hospitals throughout the country due to acute stroke or TIA. This survey provides nationwide data on hospital management of acute stroke and TIA from a mixture of all primary, secondary and tertiary medical centers operating in Israel. During the 2 month survey, nearly 2,200 patients were admitted due to an acute cerebrovascular event, yielding an estimate of about 13,000 patients admitted annually, of whom about 1,000 are due to ICH. The mean length of hospital stay was 8 days, suggesting that over 100,000 bed-days are needed annually for acute cerebrovascular disease.

During the 2 month survey, about 1,800 patients were admitted with an acute stroke (excluding TIAs), not less than the number of admissions for acute myocardial infarction ($n=1,683$) found in a national survey conducted among internal medicine and cardiac departments in Israel in 2000 [7]. Moreover, substantially more women were admitted with acute stroke than with myocardial infarction in the two corresponding national surveys (817 vs. 451), suggesting that acute stroke comprises the major vascular burden for women in Israel. The overall 30 day mortality rates for acute myocardial infarction were 11% [7] in comparison with 30% for ICH and 9% for ischemic stroke in the current survey. Mortality data, however, underestimate the true burden of stroke because, in contrast to myocardial infarction, the major burden of stroke lies in the severe chronic disability associated with it. Two-thirds of patients with ICH and 40% of patients with ischemic stroke died or had severe disability at hospital discharge, revealing the particularly high burden of cerebrovascular diseases. An important limitation of this survey is that currently data on long-term disability by accepted detailed scales are lacking.

Evidence-based guidelines and performance indicators for quality stroke care were established by expert panels [8–11]. Performance rates of brain CT and use of antithrombotic agents were relatively high. The results of this first national survey, however, underscore the discordance between clinical guidelines and current practice, and highlight specific areas for which the current organization of stroke care is deficient.

Multiple randomized clinical trials and a systematic review

have demonstrated the utility of stroke units in lessening mortality and morbidity from stroke [11–14]. Stroke units are highly cost-effective and are regarded as the highest priority for providers of a stroke service. Authoritative recommendations were issued stating that stroke care should take place in the setting of a stroke unit. In the current study, however, only 7% of patients were admitted to a department with a dedicated stroke unit, underscoring the lack of current infrastructure for stroke unit care. Several national bodies have recommended and implemented national networks of stroke units and comprehensive stroke systems [2,4,5,15–17]. Improved outcome and higher adherence to guidelines were observed in patients treated in a setting of a newly established dedicated stroke unit in Israel, demonstrating the effectiveness of stroke unit care in routine clinical practice [18].

Reperfusion of the occluded brain artery using intravenous recombinant tissue-type plasminogen activator constitutes a proven and efficacious therapy of acute ischemic stroke, within the first 3 hours of stroke onset. During the survey, however, only 0.5% of patients with acute ischemic stroke received intravenous or intraarterial thrombolytic therapy. In a survey in Canada the corresponding rate was 7% [9]. The recent approval of rt-PA therapy for treatment of acute ischemic stroke in Israel highlights the need for organized urgent stroke care that can be available for patients afflicted with acute stroke. Currently, the knowledge of stroke symptoms among the Israeli population is poor [19], indicating the need for public education regarding the warning signs of stroke and the need for immediate presentation to hospital by emergency medical services in case of sudden onset of stroke symptoms. Urgent thrombolytic therapy can be provided effectively and safely for acute ischemic stroke in Israel, in the setting of a stroke unit and acute stroke team [20].

Diagnostic tests to determine stroke etiology were seldom performed in-hospital, comparable to those found in a prior survey of 616 patients with acute stroke admitted to seven large general hospitals [21]. Carotid duplex, for example, was performed in less than a third of patients with ischemic events and in 38% of patients with TIA. Rates were not substantially higher for carotid duplex after excluding posterior circulation events or even for the performance of any type of vascular imaging study during hospitalization. Non-invasive imaging tests such as CT or MR angiography were performed in 2% of cases. In Canada, for comparison, carotid duplex was performed in 80% of cases [9]. Early investigation for the etiology of the ischemic event is particularly important, given the very high rate of early recurrent stroke after a TIA or minor stroke and the benefit of early intervention, e.g., for high grade symptomatic carotid stenosis [22,23]. Warfarin is the treatment of choice for secondary prevention in patients with atrial fibrillation [24], but was prescribed at hospital discharge to only about half the patients with atrial fibrillation after an ischemic stroke or TIA. These

rt-PA = recombinant tissue-type plasminogen activator

indicators highlight the need to improve preventive measures in-order to reduce the incidence and burden of stroke.

Data from large registries are very helpful in assessing guideline implementations in routine clinical practice. The survey findings reveal the high burden of acute cerebrovascular disease as well as the limited extent by which evidence-based guidelines for acute stroke in Israel are adopted and adhered to, and high-light specific areas for which reorganization is imperative in the health systems available for patients afflicted with acute stroke.

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Correspondence: Dr. D. Tanne, Stroke Center, Dept. of Neurology, Sheba Medical Center, Tel Hashomer 52621, Israel.
Phone: (972-3) 530-2069
Fax: (972-3) 635-6087
email: tanne@post.tau.ac.il

APPENDIX

The National Acute Stroke Israeli Survey 2004 Study Group

Survey Associates	The Neurovascular Group of the Israel Neurological Association The Israel Neurological Association The Israel Society of Internal Medicine The Israel Center for Disease Control (ICDC), Ministry of Health
Under the auspices of	The Committee of Cerebrovascular Disease, National Council of Health The Israel Medical Association
Principal Investigators	D. Tanne MD, N.M. Bornstein MD
Executive committee	D. Tanne MD, U. Goldbourt PhD, S. Koton PhD, E. Grossman MD, N. Koren-Morag PhD, M.S. Green MD PhD, N.M. Bornstein MD
Data Management Center	The Israel Society for the Prevention of Heart Attacks (ISPHA): S. Behar MD, A. Sandach MSc, R. Schwartz BSc, M. Benderly PhD
Quality Assurance and Adjudication of Cases	D. Tanne MD, R. Tsabari MD, N.M. Bornstein MD
Supported by	The Israel Center for Disease Control (ICDC), Ministry of Health, MSD, Pfizer, Sanofi-Aventis, Teva

Centers and Investigators

Assaf Harofeh Medical Center, Zrifin Barzilai Medical Center, Ashkelon Bikur Cholim Hospital, Jerusalem Bnei-Zion Medical Center, Haifa	J.M. Rabey MD, I. Kimiagar MD, E. Shevtsov MD R. Milo MD, L. Turiamsky MD I. Korn-Lubetzki, MD M. Ayed MD, B. Weller MD, L. Kaplan MD
Carmel Medical Center, Haifa HaEmek Medical Center, Afula Hadassah University Hospital, Ein Kerem, Jerusalem Hadassah University Hospital, Mt. Scopus, Jerusalem Hillel Yaffe Medical Center, Hadera Holy Family Hospital, Nazareth Josephthal Medical Center, Eilat Kaplan Medical Center, Rehovot Laniado Medical Center, Netanya Maayanei HaYeshua Hospital, Bnei Brak Meir Hospital, Kfar Saba Nazareth Hospital, E.M.M.S., Nazareth Poriyah Hospital, Tiberias Rabin Medical Center (Golda Campus), Petah Tiqva Rabin Medical Center (Beilinson Campus), Petah Tiqva Rambam Medical Center, Haifa Rebecca Sieff Medical Center, Safed Shaare Zedek Medical Center, Jerusalem Sheba Medical Center, Tel Hashomer	S. Honigman MD, H. Rawashdeh MD I. Bloch MD, A. Reshef MD O. Abramsky MD, G. Raphaeli MD Z. Weiner MD, D. Lavie MD R. Carasso MD, M. Sarkantus MD W. Nseir MD, A. Shaheen MD T. Arad MD, M. Wallid MD M. Kushnir MD, D. Gurvich MPH S. Hadar MD I. Shraga MD N. Gadoth MD, G. Vainstein MD A. Saher MD V. Vaispapir MD, K. Khazim MD Y. Streifler MD, N. Roizen MD E. Melamed MD, I. Artmanov MD D. Yarnitsky MD, G. Telman MD, E. Figlin MD R. Shahien MD, L. Lerner MD Y. Finkelstein MD PhD, M. Dano MD J. Chapman MD, D. Tanne MD, R. Tsabari MD, O. Merzeliak MD, T. Phillips RN A. Gurevich MD C. Hallevy MD, Y. Piven MD N.M. Bornstein MD, A. Gur MD PhD, I. Bova MD PhD, I. Shopin MD, I. Pfeffer BA B. Gross MD, O. Azrillin MD, Y. Kornberg RN M. Sadeh MD, Y. Lampl MD
Shmuel Harofeh Hospital, Be'er Ya'akov Soroka Medical Center, Beer Sheva Sourasky Medical Center, Tel Aviv	
Western Galilee Medical Center, Nahariya Wolfson Medical Center, Holon	