Section Editors
Johan A. Aarli, MD
Oded Abramsky, MD, PhD, FRCP

Global Perspectives

David Tanne, MD
Silvia Koton, PhD
Natan M. Bornstein, MD

Correspondence to
Dr. Tanne:
tanne@post.tau.ac.il

NATIONAL STROKE REGISTRIES: WHAT CAN WE LEARN FROM THEM?

Stroke is a major cause of long-term adult disability, death, and health care costs worldwide. This overwhelming burden on global health necessitates ongoing improvements in stroke management. Considerable progress in stroke care is now evident as a result of better prevention measures and the increasing use of acute stroke units, urgent triage, multimodal CT- or MRI-based brain imaging, and IV and endovascular reperfusion therapy.

Randomized controlled trials (RCT) have been rightly put on top of hierarchies of evidence for assessing the efficacy of therapeutic interventions. RCT, however, also have some inherent shortcomings that leave a clear need for complementary registry research. While efficacy is best evaluated in RCT, registries are most useful for the appraisal of clinical effectiveness and long-term effects of treatments in heterogeneous populations of patients, as well as for the evaluation of implementation and adherence to clinical guidelines.[1] Registries provide real-world views of clinical practice contributing to an ongoing process of quality improvement and education. They are useful for determining the presence of disparities in health care delivery among subpopulations and to assess trends in the utilization of novel technologies and quality of care.

In the last decade, registries have been gaining increasing visibility within stroke research. Registries across the globe are actively examining many aspects of stroke care. The longest-running nationwide registry collecting data on quality of care is the Risks-Stroke, the Swedish Stroke Register, established in 1994. Data from this registry reveal, for example, the steep decrease in the rates of use of high-dose heparin between 1999 and 2007, followed by a plateau, and the parallel increase in rates of thrombolytic therapy since 2003.[2]

The Performance, Effectiveness, and Costs of Treatment episodes (PERFECT) stroke registry in Finland is an example of a registry using multiple sources of national electronic individual patient-level information to produce a national stroke database with comprehensive follow-up of all hospital-treated stroke patients nationwide. It also allows for continuous monitoring of some performance indicators and stroke costs that serve as the basis for national policy decision-making. Based on this registry, the survival of Finnish ischemic stroke and intracerebral hemorrhage patients was found to improve over a decade and specialized acute care was associated with improved outcome.[3] Such a registry has substantially lower maintenance costs, yet it lacks some imperative data on in-hospital processes. The European Register of Stroke (EROS) project is a multinational population-based study in selected European centers without age restriction and using uniform standardized criteria. It allows for studying differences in patient and health care characteristics that may explain dissimilarities in risks and stroke outcomes between communities.[4]

In Israel, the National Acute Stroke ISraeli (NASIS) registry is conducted triennially during 2-month periods and includes all adult patients with acute stroke or TIA hospitalized in all medical centers nationwide. Improvements in stroke management in Israel are evident. Use of CT or magnetic resonance angiography increased from 2% in 2004 to 17% in 2010; there was a more than 10-fold rise in the utilization of reperfusion therapy for acute ischemic stroke (from 0.5% to 5.9%) with a nearly 30-fold increase among patients arriving in the first hours after symptoms onset. Concomitantly, a decrease from 9% to 6% in the rate of in-hospital mortality was observed among stroke patients.[5] The registry offers medical centers a means of evaluation of their adherence to clinical guidelines and provides the Israeli health authorities with information crucial for the planning of services and for formulating policy recommendations.

The Get With The Guidelines (GWTG)–Stroke program, developed by the American Heart Association/American Stroke Association, is the largest registry and performance improvement program for hospitalized stroke and TIA patients. During its first 6 years (2003–2009), data on 1 million patients with stroke and TIA admitted to 1,392 hospitals were collected.[6] Although this is not a nationwide registry,

From the Comprehensive Stroke Center and Department of Neurology (D.T.), Chaim Sheba Medical Center, Tel Hashomer; Sackler Faculty of Medicine (D.T., S.K., N.M.B.), Tel-Aviv University; and Neurology Department and Stroke Unit (N.M.B.), Tel Aviv Sourasky Medical Center, Israel.
Go to Neurology.org for full disclosures. Funding information and disclosures deemed relevant by the authors, if any, are provided at the end of the article.

owing to its size, broad geographic scope, duration, and prospective collection of data, it allows for the study of patient characteristics, treatments, quality indicators, and in-hospital outcomes in a very large cohort of patients. Patients from every state in the United States are represented; however, since it is voluntary and not a national or community-based registry, hospital- and patient-level selection bias is possible. Lately, the representativeness of the patient population targeted by GWTG–Stroke was shown for Medicare beneficiaries, providing evidence to support the premise that the program is representative of elderly patients with stroke and helping to justify the generalization of the registry's findings to the national level.

In China, where the annual stroke mortality rate is approximately 157/100,000, stroke has become the leading cause of death. The Chinese National Stroke Registry of hospitalized patients with acute cerebrovascular events, initiated in 2007, includes 132 hospitals, 1% of the total 13,372 general hospitals in China.[7] The registry provides information on the epidemiology of stroke, diagnosis, management, and prevention strategies, all crucial for the ongoing effort of providing and improving stroke care in a country where stroke presents an enormous health burden. In Korea, based on a nationwide hospital-based stroke registry, during the first decade of the 21st century, patient age has increased, risk factors profile and distribution of etiologic subtypes have changed, and rates of reperfusion therapy increased from 5.3% to 7.0%. These changes have been related to the increased lifespan, Westernized lifestyle, and improved public awareness.[8]

Since the implementation of thrombolysis, various aspects of the therapy have been addressed in reports based on stroke registries. The translation of information from RCT into clinical practice has been monitored. For example, data from the Risk-Stroke registry demonstrate that following the European Cooperative Acute Stroke Study (ECASS) III RCT and meta-analyses establishing the efficacy of IV recombinant tissue plasminogen activator (rtPA) in the 3- to 4.5-hour window, there has been a rapid nationwide dissemination of thrombolysis treatment in this time window, whereas the extended time window has not increased the length of door-to-needle time. The Safe Implementation of Thrombolysis in Stroke (SITS) register is an international collaboration based at the Karolinska University Hospital in Sweden. Reports from this large registry have confirmed that IV rtPA is safe and effective in routine clinical use. Furthermore, comparing data in this large registry with findings for nonthrombolyzed controls provided an opportunity to assess how the efficacy of treatment extends to populations previously not well-represented in RCT such as the elderly or those with concomitant diabetes mellitus and prior stroke.[9] Analyses from GWTG–Stroke have found that the use of IV rtPA among warfarin-treated patients with international normalized ratio ≤ 1.7 was not associated with increased risk of a symptomatic intracranial bleed compared with non-warfarin-treated patients.[10] Furthermore, a potential for substantial undertreatment was noted, since up to half of the warfarin-treated patients who might have been eligible for reperfusion therapy were not treated.

Similar to RCT, stroke registries need to be performed with careful attention to design, analysis, and interpretation. We should remain mindful of the caveats and the potential pitfalls of relying upon observational analyses for defining treatment effects. The expanded use of registries as a tool for improving quality of care has been recommended in a policy statement published by the American Heart Association,[1] focusing on ensuring high-quality data, linking clinical registries with supplemental data and integrating with electronic health records, safeguarding privacy while reducing barriers to health care improvement, and securing adequate funding. In a period of considerable change in stroke management, maintaining current and future high-quality national and multinational stroke registries worldwide has an increasingly important role as a means for measuring the delivery, effectiveness, and efficiency of stroke care.

AUTHOR CONTRIBUTIONS

Dr. Tanne: design and conceptualization of the manuscript, interpretation of published data, drafting and critical revision of manuscript. Dr. Koton: interpretation of published data, drafting and critical revision of manuscript. Dr. Bornstein: critical revision of the manuscript. All authors gave final approval of the version to be published.

STUDY FUNDING

No targeted funding reported.

DISCLOSURE

D. Tanne is a member of the steering committee of the NASIS registry. S. Koton is a member of the steering committee of the NASIS registry. N. Bornstein is a member of the steering committee of the NASIS registry. Go to Neurology.org for full disclosures.

REFERENCES

1. Bufalino VJ, Masoudi FA, Stranne SK, et al. The American Heart Association's recommendations for expanding the applications of existing and future clinical registries: a policy statement from the American Heart Association. Circulation 2011;123:2167–2179.
2. Asplund K, Hulter Asberg K, Appelros P, et al. The Riks-Stroke story: building a sustainable national register for quality assessment of stroke care. Int J Stroke 2011;6:99–108.
3. Meretoja A, Kaste M, Roine RO, et al. Trends in treatment and outcome of stroke patients in Finland from 1999 to 2007. PERFECT Stroke, a nationwide register study. Ann Med 2011;43(suppl 1):S22–S30.
4. Heuschmann PU, Wiedmann S, Wellwood I, et al. Three-month stroke outcome: the European Registers of Stroke (EROS) investigators. Neurology 2011;76:159–165.

5. Tanne D, Koton S, Molshazki N, et al. Trends in management and outcome of hospitalized patients with acute stroke and transient ischemic attack: the National Acute Stroke Israeli (NASIS) registry. Stroke 2012;43:2136–2141.
6. Fonarow GC, Reeves MJ, Smith EE, et al. Characteristics, performance measures, and in-hospital outcomes of the first one million stroke and transient ischemic attack admissions in get with the guidelines-stroke. Circ Cardiovasc Qual Outcomes 2010;3:291–302.
7. Liu L, Wang D, Wong KS, Wang Y. Stroke and stroke care in China: huge burden, significant workload, and a national priority. Stroke 2011;42:3651–3654.
8. Jung KH, Lee SH, Kim BJ, et al. Secular trends in ischemic stroke characteristics in a rapidly developed country: results from the Korean stroke registry study (secular trends in Korean stroke). Circ Cardiovasc Qual Outcomes 2012;5:327–334.
9. Mishra NK, Ahmed N, Davalos A, et al. Thrombolysis outcomes in acute ischemic stroke patients with prior stroke and diabetes mellitus. Neurology 2011;77:1866–1872.
10. Xian Y, Liang L, Smith EE, et al. Risks of intracranial hemorrhage among patients with acute ischemic stroke receiving warfarin and treated with intravenous tissue plasminogen activator. JAMA 2012;307:2600–2608.

This Week's *Neurology*® Podcast

Migraine and structural changes in the brain: A systematic review and meta-analysis **(See p. 1260)**

This podcast begins and closes with Dr. Robert Gross, Editor-in-Chief, briefly discussing highlighted articles from the October 1, 2013, issue of *Neurology*. In the second segment, Dr. Jennifer Bickel talks with Dr. Messoud Ashina about his paper about migraine and structural changes in the brain. Next, Dr. Adam Numis reads our e-Pearl of the week about manganese poisoning. Finally, Dr. Mark Keegan focuses his interview with Dr. Paul O'Connor on teriflunomide for the treatment of multiple sclerosis. Disclosures can be found at www.neurology.org.

At www.neurology.org, click on the "RSS" in the Neurology Podcast box to listen to the most recent podcast and to subscribe to the RSS feed.

CME Opportunity: Listen to this week's *Neurology* podcast and earn 0.5 AMA PRA Category 1 CME Credits™ by answering the multiple-choice questions in the online podcast quiz.

National Stroke Registries: What can we learn from them?

David Tanne, Silvia Koton and Natan M. Bornstein

Neurology 2013;81;1257-1259
DOI 10.1212/WNL.0b013e3182a6ca52