Home-Time as a Surrogate Marker for Functional Outcome After Aneurysmal Subarachnoid Hemorrhage

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Background and Purpose—Commonly used tools to determine functional outcome after aneurysmal subarachnoid hemorrhage (aSAH) have limitations. Time spent at the patient's home has previously been proposed as a robust outcome measure after ischemic stroke. Here, we set out to validate home-time as an outcome measure after aSAH.

Methods—We examined prospectively collected data from a nationwide multicenter registry of aSAH patients admitted to a tertiary neurosurgical department in Switzerland (Swiss SOS [Swiss Study on Aneurysmal Subarachnoid Hemorrhage]; 2009–2015). We calculated mean home-time (defined as days spent at home for the first 90 days after aSAH) and 95% CIs for each category of modified Rankin Scale at discharge and 1-year follow-up, using linear regression models to analyze home-time differences per modified Rankin Scale category.

Results—We had home-time data from 1076 of 1866 patients (57.7%), and multiple imputation was used to fill-in missing data from the remaining 790 patients. Increasing home-time was associated with improved modified Rankin Scale scores at time of hospital discharge ($P<0.0001$) and at 1-year follow-up ($P<0.0001$). Within each of the 8 participating hospitals, the relationship between home-time and modified Rankin Scale was maintained.

Conclusions—Home-time for the first 90 days after aSAH offers a robust and easily ascertainable outcome measure, discriminating particularly well across better recovery levels at time of hospital discharge and at 1-year follow-up. This measure complies with the modern trend of patient-centered healthcare and research, representing an outcome that is particularly relevant to the patient.

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The accurate determination of a patient's outcome is essential for clinical work and research but remains particularly difficult after aneurysmal subarachnoid hemorrhage (aSAH) as the incidence of neuropsychological and psychosocial difficulties is high in this population.[1–3] Today, basic disability scales are most frequently used as primary outcome measures,[4,5] of which the modified Rankin Scale (mRS) has been shown to have the best discriminative power.[6] Because most randomized trials for aSAH have had neutral results, however,[7,8] these scales may be insensitive to detect differences in functional outcome. In addition, interrater variability issues are well recognized.[4,9]

With the intention of overcoming the weaknesses of conventional disability scales, Quinn et al[10] previously proposed home-time as a novel outcome measure after ischemic stroke. Home-time describes the duration a patient lives in the community and has been demonstrated to accurately reflect disability after ischemic stroke in a prospective sample of n=1717 patients.[10] Moreover, its reliability and validity for ischemic stroke was subsequently reproduced.[5,11]

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Given these promising findings, the National Institutes of Health/National Institute of Neurological Disorders and Stroke Common Data Elements group has selected home-time as an exploratory outcome measure for aSAH.[12] The relationship between home-time and one of the highly recommended outcome measures for SAH patients remains to be demonstrated, however. In this context, it appears reasonable to validate home-time as a surrogate marker for post-aSAH disability.

Methods

The data that support the findings of this study are available from the corresponding author on reasonable request.

Patient Identification

We analyzed prospectively collected anonymized data recorded in a nationwide multicenter registry (Swiss SOS [Swiss Study on Aneurysmal Subarachnoid Hemorrhage]; http://www.swiss-sos.ch).[13] All patients with spontaneous SAH and evidence of an intracranial aneurysm as a source of hemorrhage were included.

Ethical Considerations and Data Collection

Each local institutional review board approved the study, under supervision of the Geneva Ethics Committee Board (No. 11-233R, NAC 11-085R). Information on variable definitions, real-time data entry, monitoring, and good clinical practice-conformal storage (Secutrial platform) has been previously described elsewhere.[14]

Study Cohort and Statistical Considerations

We used the locked 2009 to 2015 dataset,[14] extracting the dates of hemorrhage, admission, discharge, and return home. Home, in this context, included the patient's own or a relative's home but—in contrast to the original definition[10]—also included a (temporary) nursing home if return to one's previous home was not or not yet possible. Home-time at 90 days after aSAH was calculated. A 90-day cut-off was selected as this has become standard in stroke trials and to comply with the original report.[10,12] We did not consider hospital readmissions, as this information was not available. Disability outcome (mRS) was rated by a team of experienced cerebrovascular surgeons or interventional neuroradiologists trained and mostly certified in its use. These physicians were not blinded for home-time, but the decision to analyze the relationship between home-time and the mRS was made in retrospect after data collection had been completed.

With home-time data missing at random in a subset of patients (Table I in the online-only Data Supplement), multiple imputation (MI) was used to complete the dataset. The advantage was that we did not have to lose information from patients with missing data.[15] We chose 20 MI sets and the imputation mechanism based on the following variables: mRS at discharge, age, sex, and hemorrhage severity. We then derived MI estimates of mean home-time and 95% CIs for each mRS category. MI linear regression models were used to analyze differences in home-time per mRS category at time of hospital discharge and 1-year follow-up. Sensitivity analyses were also performed.

The software used for all statistical analyses was Stata v14.2 (College Station, TX) and P values <0.05 were considered statistically significant.

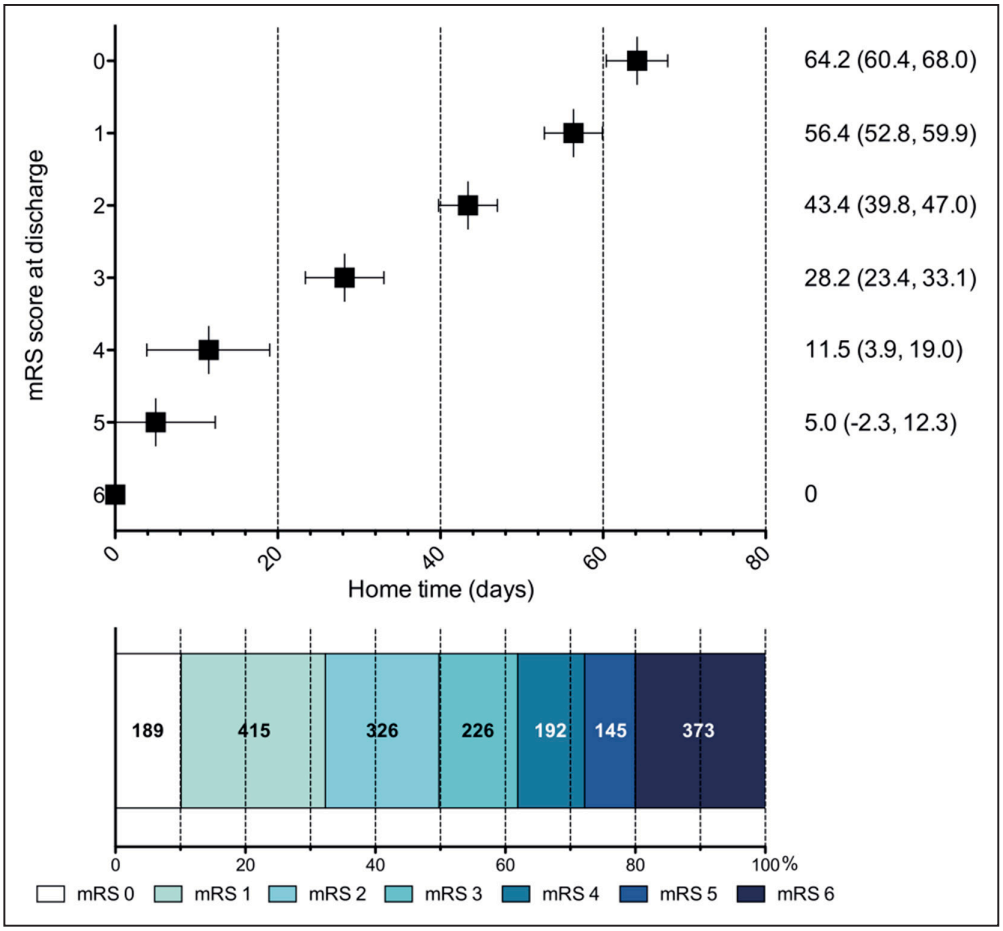

Figure 1. Forest plot of mean 90-d home-time (with 95% CIs) against modified Rankin Scale (mRS) at time of hospital discharge in N=1866, of which mRS 0=189, mRS 1=415, mRS 2=326, mRS 3=226, mRS 4=192, mRS 5=145, and mRS 6 (death)=373; P<0.0001 analyzing differences across mRS categories. Overlapping 95% CIs indicate a lack of discriminative capacity for mRS categories 4 and 5.

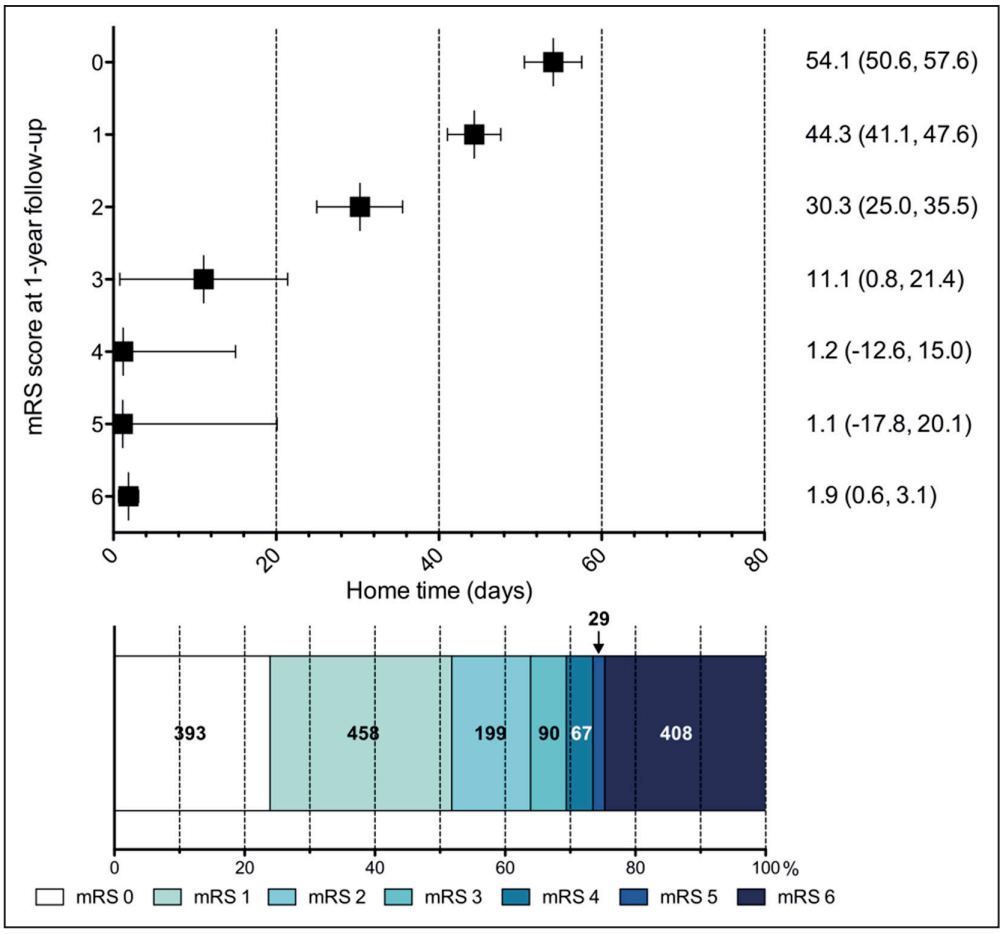

Figure 2. Forest plot of mean 90-d home-time (with 95% CIs) against modified Rankin Scale (mRS) at time of 1-y follow-up in n=1644, of which mRS 0=393, mRS 1=458, mRS 2=199, mRS 3=90, mRS 4=67, mRS 5=29, and mRS 6 (death)=408; *P*<0.0001 analyzing differences across mRS categories. Overlapping 95% CIs indicate lack of discriminative capacity for mRS categories 3 and 4, 4 and 5, and 5 and 6.

Results

A total of N=1866 patients (comprising n=1222 female, 65.5%) with a mean age of 55.8 years (±13.4 SD) were available for analysis; further patient characteristics are detailed in Table I in the online-only Data Supplement. Mean time in hospital was 21.1 days (±13.5 SD), and mean home-time was 57.7 days (±39.9 SD).

Home-time was significantly associated with mRS score at discharge (*P*<0.0001). On analysis of between-category differences, home-time was significantly associated with mRS category, in particular across the better recovery levels (mRS 0–4, all *P*<0.001; Figure 1). Overlapping 95% CIs indicate a lack of discrimination between the mRS categories 4 and 5 (*P*=0.114).

Home-time was significantly associated with mRS score at 1-year follow-up (*P*<0.0001). On analysis of between-category differences, home-time was significantly associated with mRS category across the better recovery levels (mRS 0–3; all *P*<0.001; Figure 2). Overlapping 95% CIs indicate a lack of discrimination between mRS categories 3 and 4 (*P*=0.089), 4 and 5 (*P*=0.993), and 5 and 6 (*P*=0.916).

This relationship between home-time and mRS held both within each of the 8 participating hospitals (all *P*<0.0001) and within the original (nonimputed) dataset, although with wider CIs, as expected (*P*<0.0001; Tables II and III in the online-only Data Supplement).

Discussion

This study set out to validate home-time as a surrogate marker for functional outcome after aSAH. As previously shown for ischemic stroke,[5,10,11] we were able to demonstrate that home-time is significantly associated with post-aSAH disability as measured by the mRS, particularly across better recovery levels. Given that mRS represents the current "gold-standard" for outcome measurement after aSAH and stroke,[5,12,16] our findings provide strong evidence of the validity of home-time as a potential outcome measure.

The particular strengths of home-time over conventional disability grading scales are numerous, including (1) objective measure versus subjectively estimated category, (2) nearly perfect reliability versus high interobserver variability,[4,9] (3) standard variable from the patient chart versus complex and abstract score requiring official training and certification. A further strength of home-time is that it can be assessed immediately and is easily comprehensible, even by nonmedical personnel, such as the patient, relatives, or the public.[10]

Patient data in the Swiss SOS registry is representative of the general aSAH population, encompassing the whole range

of aSAH case severities. As can be seen from Figures 1 and 2, home-time was less valid as an outcome measure in the more disabled population, however (in particular mRS 4 and 5). This probably reflects the fact that patients for whom no rehabilitation potential is expected because of severe brain injury (mRS 5) are sometimes discharged home (with professional support) earlier than patients with moderately severe disability (mRS 4) who may benefit from longer in-patient rehabilitation. The fact that we included discharge to nursing facilities in the home-time calculation but did not account for hospital readmissions may have added to this effect.

The strengths of the present study include the prospective collection of a relatively large, multicenter dataset. In addition, result presentation was deliberately handled in a similar manner to the original report[10] to allow the comparison of home-time in aSAH and ischemic stroke patients across disability levels. In contrast to the prior study,[10] the Swiss SOS dataset also contained information on the 1-year disability outcome, allowing us to display the association between home-time and long-term outcome as well (Figure 2).

The key weakness of this study is the missing data burden. As there was no obvious mechanism behind the missing data (=missing at random), we used MI to account for this problem, but it should be emphasized that even the most exact calculations can never replace a complete dataset.[15] Also, home-time depends largely on the availability of dedicated in-patient rehabilitation centers. As such, it is difficult to generalize the present findings to other countries and settings. In particular, they may not be applicable to countries with less developed health systems. Finally, the definition of home-time was slightly modified in our study but should be in accordance with the original description, when possible.[10]

Summary

Home-time for the first 90 days after aSAH offers a robust and easily ascertainable outcome measure, discriminating particularly well across better recovery levels at time of hospital discharge and at 1-year follow-up. This measure complies with the modern trend of patient-centered healthcare and research, representing an outcome that is particularly relevant to the patient.

Appendix: List of Contributors to the Swiss SOS Study Group

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Disclosures

None.

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