Years of Optimum Health Lost Due to Complications After Acute Ischemic Stroke
Disability-Adjusted Life-Years Analysis
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Background and Purpose—Complications after stroke increase disability or death. The disability-adjusted life-year (DALY) metric, developed by the World Health Organization to measure the global burden of disease, integrates both mortality and disability. Widely used in population-level data analyses, it has not been applied to individual patient-level data captured in outcome registries.

Methods—We analyzed patient-level data from the outcome registry of 1254 consecutive patients with acute ischemic stroke enrolled between September 1, 2004, and August 31, 2005, in South Korea. For each subject, we calculated DALY lost due to the qualifying stroke and then analyzed additional DALY lost due to complications after stroke.

Results—For 1233 patients with available 3-month outcomes, the average DALY lost due to the index stroke was 3.82 (95% CI, 3.68 to 3.96). Any complications, neurological complications, and medical complications occurred in 34.0%, 20.8%, and 24.0%, respectively. The additional DALYs lost associated with any, neurological, and medical complications were 2.11 (95% CI, 1.78 to 2.44), 2.15 (95% CI, 1.72 to 2.59), and 1.99 (95% CI, 1.59 to 2.40), respectively. Patients with 1 complication had 1.52 (95% CI, 1.15 to 1.89) additional DALY lost, and those with ≥2 complications had 2.69 (95% CI, 2.18 to 3.20) additional DALY lost.

Conclusion—Early poststroke complications deprive patients of approximately 2 years of optimum health. Greater numbers of complications are associated with greater loss of healthy life-years. DALY analysis quantifies the burden of poststroke complications with a uniform metric potentially useful for health system planners. (Stroke. 2010;41:00-00.)

Key Words: acute ischemic stroke ■ complications ■ DALY ■ outcome

Early poststroke complications can cause increased disability and mortality.1–4 Acute stroke management guidelines strongly recommend an organized system of patient stroke care to prevent or minimize complications. Because well-organized stroke care requires allocating human and structural resources, health professionals caring for patients with stroke must delineate for public and health policy decision-makers the impact on population health of poststroke complications and the benefits organized stroke care offers by averting them. Burden of disease metrics that are applicable across multiple disease states facilitate health policy planning, but prior studies have not characterized poststroke complications with these measures.

To date, the adverse impact of complications on stroke outcome has generally been assessed using effect on mortality or on a dichotomized, stroke-specific measure of functional outcome.1–4 Given that complications increase not only mortality, but also disability, mortality measures alone are insufficient to delineate the full impact of poststroke complications. Stroke-specific disability measures have limited comparability to other disease states. Moreover, dichotomized analysis of these measures collapses distinct disability levels into only 2 outcome categories and discards substantial information captured by the original, fine-grained disability state distinctions. Because poststroke complications can alter patient outcome anywhere along the spectrum of disability,
dichotomized analysis assessing only a single health state transition will often underestimate their full adverse impact. Furthermore, the common reporting of findings using ORs (increased odds of mortality or worse outcome) does not provide the lay public and health policy decision-makers with an actionable direct measure of the magnitude of the health burden introduced by poststroke complications and is accordingly less appealing to lay public and health policy decision-makers.

Calculating disability-adjusted life-years (DALY) lost is a promising approach to characterizing the health impact of poststroke complications. The DALY system was developed by the World Health Organization to measure the global burden of hundreds of diseases and injuries with a common metric. Subsequently, the DALY approach has been used to analyze the efficacy of health interventions at a population level. The DALY metric integrates both mortality (years of life lost [YLL] due to premature death) and disability (years of healthy life lost due to living with disability [YLD]). One DALY lost is a loss of 1 year of optimum health free of disability. Because time of healthy life lost is an intuitively accessible concept applicable across many disease states, the DALY metric is well suited to provide a useful measure of the impact of poststroke complications and organized stroke care.

The objective of this study was to apply the DALY metric to quantify the additional healthy life-years lost due to complications after acute ischemic stroke.

Patients and Methods

Patients

The study population comprised patients enrolled in the Complication in Acute Stroke Study (COMPASS). COMPASS was a multicenter, prospective, observational study that evaluated poststroke complications and 3-month functional outcomes for all consecutive patients with acute ischemic stroke admitted to 4 university hospitals of South Korea from September 1, 2004, to August 31, 2005. During the study period, primary stroke centers were not designated in South Korea, and the participating university hospitals played a role of primary stroke centers. Eligibility criteria were: (1) clinical diagnosis of a new-onset clinical ischemic stroke lasting >24 hours or reversed by reperfusion therapy; (2) neuroimaging findings consistent with ischemic stroke; and (3) admission within 7 days from stroke onset. The study was approved by the Institutional Review Boards of participating institutions.

For each patient, data were prospectively collected by a predetermined protocol, including baseline demographics, stroke severity as indexed by the National Institutes of Health Stroke Scale (NIHSS), stroke subtype (Trial of ORG 10172 in Acute Stroke Treatment classification), laboratory data, postadmission neurological and medical complications, and final 3-month functional outcomes as measured by the modified Rankin Scale (mRS) of global disability. Responsible physicians evaluated NIHSS at admission, 1, 2, 3, 7, and 14 days, or until discharge and at the time of any neurological deterioration. Trained research nurses evaluated 3-month mRS outcomes using a structured format. The 3-month mRS outcomes were available for 1233 (98.3%) patients; the mRS outcomes were obtained by direct interview for 831 (66.3%) and by telephone interview for 423 (32.0%) patients. The neurological and medical complications were collected and evaluated by responsible physicians and research nurses.

Neurological complications included ischemic stroke progression, symptomatic hemorrhagic transformation, recurrent stroke, and seizure within 2 weeks from stroke onset. Medical complications included pneumonia, myocardial infarction, urinary tract infection, extracranial bleeding, pulmonary embolism, pyrexial illness, pressure sore, fall, and others within 4 weeks from stroke onset. Definitions of the individual complications were provided in an earlier published article. Although medical complications could be assessed by a review of medical records, accurate identification of the target neurological complications required detailed, prospective neurological evaluations. For this practical reason, we had different time periods for surveillance for neurological versus medical complications.

DALY Derivation

For each patient, we calculated the DALY lost due to the qualifying stroke based on the patient’s age, gender, and 3-month mRS using previously published methodology. Briefly, DALY lost was derived from the formula DALY = YLL + YLD, where YLL is the years of life lost due to premature death and YLD is the years of healthy life lost due to disability. YLL and YLD were derived by the following formulas:

\[
YLL[K, r, K] = \frac{DKC e^{-\beta(r + \beta)}[\beta e^{-r(r + \beta)L_d + A_s} - (r + \beta)(L + A)] - 1}{(1 - K)r[1 - e^{-r}]} \\
YLD[K, r, K] = \frac{DKC e^{-\beta(r + \beta)}[\beta e^{-r(r + \beta)L_d + A_s} - (r + \beta)(L + A)] - 1}{(1 - K)r[1 - e^{-r}]} \\
\]

in which \(K\) indicates age-weighting modulation factor (\(K = 1\) or 0); \(\beta\), parameter from age weighting function (\(\beta = 0.04\) or 0); \(r\), discount rate (\(r = 0.03\) or 0); \(C\), constant (\(C = 0.1658\)); \(A\), age of death; and \(L\), life expectancy of general population at age \(A\).

\(D\) indicates disability weight; and \(A_s\), age at stroke; \(L_d\), duration of disability with a mRS×state (=life expectancy of a stroke patient with a mRS×disability at age \(A_s\)).

The discount rate \(r\) reflects the standard health policy modeling assumption that values a year of healthy life lost in the future less than a year of healthy life lost in the immediate present, setting the discount rate to 3% annually. The age-weighting factors (\(K\), \(\beta\)) reflect another assumption that assigns different values to different years of life, higher in young adult ages than in infancy or old age.

The YLL is conceptually the loss of life expectancy of general population at age \(A\): YLL = L. The YLD is conceptually the difference between healthy life-years (disability weight of zero) and life-years of living with disability.

For stroke survivors, years that they will live with disability must be estimated, taking into account that studies have shown that long-term life expectancy decreases monotonically as mRS level increases. Mortality hazard ratios specific to each mRS level were used derived in a prior study. By applying the mRS-specific mortality hazard ratios to the age-specific mortality rates provided in life tables for the general Korean population, the age-specific life expectancies and expected death ages for each patient, given their mRS level, were determined. In this study, general population life expectancies were taken from the 2005 Korean life table.

Two case examples are presented. If a 68.5-year-old Korean woman has a fatal stroke (mRS 6), YLL = 8.11. If a 68.5-year-old Korean woman has a stroke with a 3-month mRS of 2, YLL = 2.50, YLD = 1.49, and total DALY = 3.99. (The detailed mathematical derivation is provided in the supplemental mathematical appendix available online at)http://stroke.ahajournals.org).

DALY Lost Comparison

To derive the additional DALY lost due to complications, we compared the DALYs lost of patients with complications and those...
without complications. The 3-month mRS distributions were also compared. In addition, to delineate whether patients experiencing more complications have more DALYs lost, we categorized the patients into 3 groups (no complication, 1 complication, and ≥2 complications) and compared their DALYs lost.

**Sensitivity Analyses**

There have been some ethical criticisms on applying a 3% future discount rate and age-weighting in deriving DALYs. To explore the effect of removing these assumptions, in addition to DALYs incorporating these factors (DALY[3,1]), we calculated additional sets of DALYs in which both future discounting and age-weighting were not used: DALY[0,0].

**Statistical Analysis**

The DALYs lost between patients with complications and those without complications were compared using Student t test. For comparing the DALYs lost across 3 groups categorized by complication numbers, analysis of variance was used. An analysis of covariance was used for multivariable analyses. Pearson $\chi^2$ test, Student t test, or the Mann–Whitney U test was used to compare potential prognostic factors between tested groups. We selected for entry into the multivariable models the covariates showing probability value <0.1 in the comparison of patients with and without any neurological complications or in the comparison of patients with and without any medical complications. The selected covariates were age, gender, initial NIHSS, prior stroke, potential cardioembolic source, smoking, prestroke dependence, Trial of ORG 10172 in Acute Stroke Treatment subtype, hemoglobin, albumin, glucose, and white blood cell count.

**Results**

**Population Characteristics**

During the 1-year period, a total of 1254 consecutive patients with acute ischemic stroke were prospectively recruited. The mean age (±SD) was 66.5 (±12.1) years and 703 (56.1%) patients were male. The median NIHSS score at admission was 4 (range, 0 to 32) (Table 1). For 1233 patients with available 3-month mRS outcomes, the frequencies of mRS 0 to 6 were 345 (28.0%), 276 (22.4%), 182 (14.8%), 150 (12.2%), 105 (8.5%), 84 (6.8%), and 91 (7.4%), respectively (Figure 1). For the 1233 patients, the average DALY[3,1] lost due to the qualifying stroke was 3.82 (95% CI, 3.68 to 3.96). Any complications, neurological complications, and medical complications developed in 419 (34.0%), 256 (20.8%), and 303 (25.0%), respectively. The most common specific complications were ischemic stroke progression (16.9%) and pneumonia (11.7%).

**DALY Lost Due to Complications**

Figure 1 shows the comparison of 3-month mRS distributions between patients with complications and those without complications. Complications shifted the mRS distribution with a substantial increase of patients in worse outcome categories. For the dichotomized end point of dead or dependent (mRS 3 to 6), as previously reported, poor outcomes were increased by neurological (OR, 95% CI: 5.47, 3.63 to 8.24) and medical (OR, 95% CI: 3.47, 2.30 to 5.23) complications.

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Table 1. Baseline Demographics

<table>
<thead>
<tr>
<th></th>
<th>All Patients (n=1254)</th>
<th>Neurological Complication Yes (n=264)</th>
<th>Neurological Complication No (n=990)</th>
<th>Medical Complication Yes (n=303)</th>
<th>Medical Complication No (n=951)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>66.5±12.1</td>
<td>67.4±11.5</td>
<td>66.0±12.3</td>
<td>70.6±11.1</td>
<td>64.9±12.1</td>
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<tr>
<td>Male</td>
<td>703 (56.1)</td>
<td>140 (53.0)</td>
<td>563 (56.9)</td>
<td>156 (51.5)</td>
<td>547 (57.5)</td>
</tr>
<tr>
<td>Initial NIHSS, median (IQR)</td>
<td>4.0 (2.0–8.0)</td>
<td>6.0 (3.0–14.5)</td>
<td>4.0 (2.0–7.0)</td>
<td>11.0 (5.0–18.0)</td>
<td>3.0 (2.0–6.0)</td>
</tr>
<tr>
<td>Prior stroke</td>
<td>287 (22.9)</td>
<td>53 (20.1)</td>
<td>234 (23.6)</td>
<td>87 (28.7)</td>
<td>200 (21.0)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>785 (62.6)</td>
<td>164 (62.1)</td>
<td>621 (62.7)</td>
<td>198 (65.3)</td>
<td>587 (61.7)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>428 (34.1)</td>
<td>98 (37.1)</td>
<td>330 (33.3)</td>
<td>115 (38.0)</td>
<td>312 (32.9)</td>
</tr>
<tr>
<td>Cardioembolic source</td>
<td>247 (19.7)</td>
<td>69 (26.1)</td>
<td>178 (18.0)</td>
<td>108 (35.6)</td>
<td>139 (14.6)</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>458 (35.6)</td>
<td>99 (37.5)</td>
<td>359 (36.3)</td>
<td>103 (34.0)</td>
<td>355 (37.3)</td>
</tr>
<tr>
<td>Current smoking</td>
<td>353 (28.1)</td>
<td>54 (20.5)</td>
<td>299 (30.2)</td>
<td>57 (18.8)</td>
<td>296 (31.1)</td>
</tr>
<tr>
<td>Prestroke mRS 3–5</td>
<td>87 (6.9)</td>
<td>19 (7.2)</td>
<td>68 (6.9)</td>
<td>50 (16.5)</td>
<td>37 (3.9)</td>
</tr>
</tbody>
</table>

Numbers in parentheses are percentage if not otherwise indicated. The value of a±b indicates a mean±SD. IQR indicates interquartile range.
In the DALY analysis, the patients with any complications experienced an average of 5.21 (95% CI, 4.91 to 5.52) DALYs lost, whereas those without complications experienced an average of 3.10 (95% CI, 2.98 to 3.23) DALYs lost. Consequently, any complication was associated with an additional 2.11 (95% CI, 1.78 to 2.44, P < 0.001) DALY loss (Table 2). The patients with neurological and medical complications experienced an additional DALY loss of 2.15 (95% CI, 1.72 to 2.59, P < 0.001) and 1.99 (95% CI, 1.59 to 2.40, P < 0.001), respectively. For specific complications, ischemic stroke progression and pneumonia were associated with an additional DALY loss of 2.18 (95% CI, 1.71 to 2.65, P < 0.001) and 1.99 (95% CI, 1.54 to 2.73, P < 0.001), respectively. The additional DALY lost remained significant after adjustment for baseline prognostic factors and when both the future discount rate and age-weighting were not applied. Adjustment for baseline prognostic factors reduced the complication-related additional DALY lost to a modest degree. However, when the future discounting and age-weighting were removed, the complication impact was magnified (Table 2). In addition to the significances observed in the numeric statistics, graphic analyses show that the complications shifted the distribution of DALYs lost with a substantial increase in the proportion of patients losing ≥5 DALYs due to their stroke and its aftermath (Figure 2).

More DALY Lost With More Complications

Two hundred thirty (18.7%) and 200 (16.2%) patients experienced 1 complication and ≥2 complications, respectively. The patients experiencing more complications had more DALYs lost (Table 3; Figure 3). As compared with patients without complications, those with 1 complication had 1.52 (95% CI, 1.15 to 1.89, P < 0.001) more DALYs lost, and those with ≥2 complications had 2.69 (95% CI, 2.18 to 3.20, P < 0.001) more DALYs lost. The patients with ≥2 complications had 1.18 (95% CI, 0.57 to 1.78, P < 0.001) more DALYs lost than those experiencing 1 complication. These differences remained significant after adjustment for baseline prognostic factors and when both the discount rate and age-weighting were not applied. Graphic analysis displayed the differences in the DALY lost distributions across the 3 groups (Figure 3).

Discussion

This study shows that the DALY metric delineates the excess burden of poor outcomes that can be attributed to poststroke complications in an intuitively understandable manner. Early poststroke neurological or medical complications deprived patients with acute ischemic stroke of an average of additional 2 years of optimum health. Furthermore, as patients experienced more complications, they lost more years of optimum health: 1.5 years with 1 complication and 2.7 years with ≥2 complications. The validity of our findings is supported by (1) consistent results in unadjusted and adjusted analyses; (2) robustness when both future discounting and age-weighting were used or not; and (3) comparable complication-associated outcome shifts observed in the mRS and DALY lost distributions (Figures 1 and 2).

Conventionally, dichotomized analyses have been used to evaluate the impact of complications on stroke outcome.1–4 However, the DALY metric provides additional advantages. Allocating human and structural resources to competing health interventions or programs requires a transparent and scientific comparison. Unfortunately, the variety of outcome measures used for evaluating diverse health conditions and treatments can bewilder the lay public and policy decision-makers. Health-adjusted life-year metrics, including DALYs and quality-adjusted life-years, provide a more uniform, fungible metric. However, for direct comparison of health burden and gain across disease states, DALYs offer several advantages over quality-adjusted life-years. Quality-adjusted life-years are strongly affected by the sociocultural background, disease state, and disease duration (adjustment to disease bias) of the lay informants participating in their derivation. DALYs are founded in person-tradeoff analyses made by diverse medical professionals, ensuring breadth of perspective appropriate for health policy decision-making. DALY values indicate a patient’s loss or gain of health life-years, a metric that is patient-centered and intuitively accessible. Therefore, this DALY analysis of the impact of...
poststroke complications and organized stroke care benefits can help the public and health policy decision-makers understand the imperative of organized stroke care and relevant resource allocation. For example, the current study showed that pneumonia deprives individuals of an additional 2 years of healthy life, and a prior study showed that a formal dysphagia screening and management could lead to approximately 50% relative risk reduction of pneumonia.\textsuperscript{16} Given a 5.6% incidence of pneumonia in acute stroke and an annual incidence of stroke of 795,000 in the United States,\textsuperscript{17,18} a nationwide implementation of the formal dysphagia screening and management program would save annually 44,520 (= 795,000 × 2 [years] × [0.056 to 0.028]) healthy life-years in the United States.

The adverse effects of poststroke complications span all ranges of presenting stroke severity and final outcome functional status. Interventions to prevent complications are likely to yield a benefit over all ranges of stroke severity. The degree of benefit of avoiding complication may often be modest, in contrast, for example, with the substantial benefit of early reperfusion therapy. A prior study demonstrated that analyzing shifts over outcome ranks, rather than dichoto-
mized analysis, is a more efficient statistical technique when treatments yield a small and uniform degree of benefit over all ranges of stroke severity.19 Because the DALY metric can modestly reduce it. On multivariable analyses, age and initial NIHSS were independent predictors for DALY lost due to the index stroke. Because patients with old age and severe stroke are also at high risk of complications, adjusting for these variables reduced the complications-associated DALY lost. However, the impact of neurological and medical complications on DALY lost remained robust after adjustment.

This study has several limitations. Because we recruited all patients admitted within 7 days from stroke onset, we failed to capture some complications that had already developed before admission such as ischemic stroke progression and thereby our findings might underestimate the total harm attributable to complications. This was a hospital-based study performed in 4 university hospitals. Therefore, the extrapolation of our findings to the general Korean stroke population or other populations might be limited. In addition to func-
tional disability, poststroke complications can also modify cognitive and emotional outcomes after stroke, and the neuropsychological outcomes influence poststroke long-term mortality.20 The mRS global disability measure likely incorporates some but not all aspects of cognitive and emotional outcome. Accordingly, we did not fully explore the neuropsychological impact of poststroke complications on DALY outcomes.

We applied disability-specific mortality hazard ratios derived from studies of European populations to the Korean stroke population. Ideally, the disability-specific mortality hazard ratios would have been generated from a Korean stroke cohort study, but these data were not available. Also, we used mortality hazard ratios obtained from different time periods. Although the British Lothian stroke registry and the Swedish Riks stroke registry enrolled patients during the periods 1990 to 2000 and 2001 to 2002,13,14 our patients were recruited between 2004 and 2005. Over the last decade, as vascular prevention therapies as well as general medical cares with proven efficacy have been introduced into routine clinical practice, the long-term mortality rate of stroke survivors is expected to decrease. However, we could not reflect this secular trend because of paucity of data.

In conclusion, early poststroke complications deprive a patient of an average 2 years of optimum health free of disability. Experiencing a greater number of complications is associated with losing more years of optimum health. DALY analysis quantifies the burden of poststroke complications with an intuitively accessible, directly comparable, and widely used metric. These findings can guide public policy decision-makers in resource allocation regarding organized stroke care to prevent complications of stroke.

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References

Supplemental Mathematical Appendix

The complete equations for YLL and YLD are as follows:

\[ YLL[r,K] = KCe^{(r+\beta)(A-L)} \left(1 - e^{-(r+\beta)A}ight) - e^{-(r+\beta)A} \left[-(r+\beta)(A-L) - 1\right] + \left[(1-K)r \right] \left[1-e^{-d}\right] \]

in which \( K \) indicates age-weighting modulation factor (\( K = 1 \) or 0); \( \beta \), parameter from age weighting function (\( \beta = 0.04 \) or 0); \( r \), discount rate (\( r = 0.03 \) or 0); \( C \), constant (\( C = 0.1658 \)); \( A \), age of death; and \( L \), life expectancy of general population at age \( A \).

\[ YLD[r,K] = DKCe^{(r+\beta)(A-L)} \left(1 - e^{-(r+\beta)A}ight) - e^{-(r+\beta)A} \left[-(r+\beta)(A-L) - 1\right] + \left[(1-K)r \right] \left[1-e^{-d}\right] \]

in which \( D \) indicates disability weight; \( K \), age-weighting modulation factor (\( K = 1 \) or 0); \( \beta \), parameter from age weighting function (\( \beta = 0.04 \) or 0); \( r \), discount rate (\( r = 0.03 \) or 0); \( C \), constant (\( C = 0.1658 \)); \( A_r \), age at stroke; and \( L_d \), duration of disability with a mRS\text{-}state (life expectancy of a stroke patient with a mRS\text{-}disability at age \( A_r \)).

For a 68.5-year-old Korean woman with a fatal stroke (mRS \( 6 \)),

\[ L_d = 0 \]


We assigned disability weight of 0.228 to mRS \( 2 \) status derived in a prior study.\(^4\)

\[ L = 8.72 \]

Because the death in this patient is the future event that will occur after 12.33 years, applying future discount rate is required for YLL[3,1] at age of 68.5 as shown below:\(^2\)

\[ YLL[3,1] \text{ at age of 80.5} = YLL[3,1] \times e^{0.03 \times 80.5} \]

\[ YLD[3,1] \text{ at age of 80.5} = YLD[3,1] \times e^{0.03 \times 80.5} \]

Finally, DALY[3,1] = 2.50 + 1.49 = 3.99.

Supplemental References


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