Alberta Stroke Program Early Computed Tomographic Scoring Performance in a Series of Patients Undergoing Computed Tomography and MRI

Reader Agreement, Modality Agreement, and Outcome Prediction

Ryan A. McTaggart, MD; Tudor G. Jovin, MD; Maarten G. Lansberg, MD; Michael Mlynash, MD; Mahesh V. Jayaraman, MD; Omar A. Choudhri, MD; Manabu Inoue, MD; Michael P. Marks, MD; Gregory W. Albers, MD; on behalf of the DEFUSE 2 Investigators

Background and Purpose—In this study, we compare the performance of pretreatment Alberta Stroke Program Early Computed Tomographic scoring (ASPECTS) using noncontrast CT (NCCT) and MRI in a large endovascular therapy cohort.

Methods—Prospectively enrolled patients underwent baseline NCCT and MRI and started endovascular therapy within 12 hours of stroke onset. Inclusion criteria for this analysis were evaluable pretreatment NCCT, diffusion-weighted MRI (DWI), and 90-day modified Rankin Scale scores. Two expert readers graded ischemic change on NCCT and DWI using the ASPECTS. ASPECTS scores were analyzed with the full scale or were trichotomized (0–4 versus 5–7 versus 8–10) or dichotomized (0–7 versus 8–10). Good functional outcome was defined as a 90-day modified Rankin Scale score of 0 to 2.

Results—Seventy-four patients fulfilled our study criteria. The full-scale inter-rater agreement for CT-ASPECTS and DWI-ASPECTS was 0.579 and 0.867, respectively. DWI-ASPECTS correlated with functional outcome (P=0.004), whereas CT-ASPECTS did not (P=0.534). Both DWI-ASPECTS and CT-ASPECTS correlated with DWI volume. The receiver operating characteristic analysis revealed that DWI-ASPECTS outperformed both CT-ASPECTS and the time interval between symptom onset and start of the procedure for predicting good functional outcome (modified Rankin Scale score, ≤2) and DWI volume ≥70 mL.

Conclusion—Inter-rater agreement for DWI-ASPECTS was superior to that for CT-ASPECTS. DWI-ASPECTS outperformed NCCT ASPECTS for predicting functional outcome at 90 days. (Stroke. 2015;46:407-412. DOI: 10.1161/STROKEAHA.114.006564.)

Key Words: brain ischemia, diffusion magnetic resonance imaging, multi-slice computed tomography, stroke, thrombectomy
with acute stroke who underwent endovascular therapy after MRI. The goal of our study is to compare the performance of pretreatment ASPECTS using both NCCT and MRI in a large endovascular therapy cohort.

Methods

DEFUSE 2 began as a single-center study in July 2008. After this, 8 sites in the United States and 1 site in Europe were added when National Institutes of Health funding was obtained in September 2009. Patient enrollment was completed in September 2011.

This study was approved by the Institutional Review Boards of the individual institutions. To be eligible for enrollment, endovascular therapy had to be initiated within 12 hours of symptom onset. The patients had to be adults (aged ≥18 years) and should have a National Institute of Health Stroke Scale score that was ≥5 and persistent large-vessel occlusion, despite earlier treatment with an intravenous tissue-type plasminogen activator. Inclusion criteria for this DEFUSE 2 substudy were evaluable pretreatment NCCT, DWI, and 90-day modified Rankin Scale scores.

Imaging

Head CT imaging was performed according to standard CT protocols (5-mm slice thickness without contrast, 120 kV, high tube current, parallel to the orbitomeatal line). Head MRI was performed on a 1.5 or 3.0 T MRI system. A standardized protocol including a gradient recalled echo sequence, DWI sequence, and perfusion-weighted imaging sequence was performed along with a magnetic resonance angiography study of the Circle of Willis. Image analysis was done using a rapid processing of perfusion and diffusion computer system, which generated quantitative DWI and perfusion-weighted imaging lesion maps within 4 to 7 minutes of processing time. The automated maps generated by the rapid processing of perfusion and diffusion computer system included a volume estimate of the ischemic core based on apparent diffusion coefficient thresholds.

Reader Agreement

Reader agreement was assessed or CT (CT-ASPECTS) and DWI (DWI-ASPECTS) scored by 2 readers (R.A.M. and T.G.J.), who were blinded to all clinical information except the affected hemisphere. Full-scale inter-rater agreement and dichotomized (>7 versus ≤7) and trichotomized ASPECTS (0–4 versus 5–7 versus 8–10) agreements were assessed. For our performance analysis of each modality, a third reader (M.P. Marks) adjudicated score discrepancies by choosing which score was considered to be the most accurate of the 2 readers’ scores.

Performance Analysis

We assessed the accuracy of CT-ASPECTS, DWI-ASPECTS, and stroke onset to procedure start time, for predicting good outcome. Good functional outcome (GFO) was defined as a 90-day modified Rankin Scale score of 0 to 2. DWI lesion volumes were calculated using rapid processing of perfusion and diffusion computer software (as above), and an initial DWI volume of ≥70 mL was used to define a group of patients in whom it was hypothesized that reperfusion would be futile (poor outcome regardless of successful recanalization) as suggested by previous data. The relationship between reader score differences (R1 versus R2) within each modality and the adjudicated reads between modalities (CT-ASPECTS versus DWI-ASPECTS) was assessed using a Bland–Altman plot with adjusted 95% limits of agreement. The Pearson correlation coefficient was used to test the association between the timing of the scans and discrepancies between modality scores. Trends in the rates of GFO and baseline DWI lesion volumes along the dichotomized ASPECTS were assessed using the Cochran–Armitage trend test and the Jonckheere–Terpstra test for ordered alternatives. To evaluate the predictive ability of the CT-ASPECTS, DWI-ASPECTS, and time of procedure start for each outcome (functional outcome and DWI volume), receiver operating characteristic curves were constructed. The area under the receiver operating characteristic curve (AUC) was used as a scalar measure to assess the performance of prognostic risk scores. The comparison of the AUCs was conducted by a nonparametric method. Statistical tests were performed using SAS 9.3 and IBM SPSS Statistics 20 statistical software packages.

Results

Seventy-four patients fulfilled our study criteria. The mean age was 67±15 (26–92) years, the median National Institute of Health Stroke Scale score was 17 (interquartile range, 12–20), and 47% were women. There were 42 (57%) patients with left-sided strokes. Occlusion locations were middle cerebral artery in 47 (64%) patients, internal carotid artery in 24 (32%) patients, or other in 3 (4%) patients. The median (interquartile range) time from stroke onset to CT was 1.4 (0.8–3.8) hours and to MRI was 4.2 (2.6–5.4) hours with a median time difference between CT and MRI of 1.6 hours (95% confidence interval [CI], 1.1–2.4).

Reader Agreement

Full-scale agreement (measured by the intraclass correlation coefficient) for CT-ASPECTS and DWI-ASPECTS was 0.579 and 0.867, respectively. Agreement within 1 point of the ASPECTS score was seen in 70% of the CT group and in 90% of the DWI group. Bland–Altman plots for CT and DWI reader agreements are presented in Figure 1, and dichotomized (>7 versus ≤7) and trichotomized ASPECTS (0–4 versus 5–7 versus 8–10) agreements are presented in Table 1; the agreement on CT-ASPECTS was moderate, whereas on DWI-ASPECTS, it was substantial and significantly better than the agreement on CT-ASPECTS.

Performance Analysis

The adjudicated CT and DWI scores averaged 7.6 (range, 4–10) and 7.0 (range, 0–10), respectively. CT scores were not consistently higher or lower than the MRI scores at any time interval, and there was no association between the timing of the scans and discrepancies between modality scores; the Pearson correlation between CT- and DWI-ASPECTS score differences and the time difference between scans was r=0.14 (P=0.226). In addition, there was no trend for the differences between the scores to increase or decrease in relation to the time difference between CT and MRI (P=0.31; Figure 1 in the online-only Data Supplement). Scores >7 were seen in 52.7% of CT-ASPECTS and 47.3% of DWI-ASPECTS groups. Overall agreement between modalities was 0.43 (95% CI, 0.23–0.60), and agreement decreased from the upper to the lower end of the scale (Figure 2). The sensitivity and
specificity of baseline CT-ASPECTS (using the baseline DWI-ASPECTS as the standard) are presented in Table 2.

DWI-ASPECTS trichotomized into 8 to 10, 5 to 7, and 0 to 4 score-groups correlated with functional outcome (corresponding GFO rates were 53%, 27%, and 10%; \( P=0.004 \) for this trend), whereas CT-ASPECTS did not (corresponding GFO rates were 39%, 37%, and 20%; \( P=0.534 \); Table 3). Both DWI-ASPECTS and CT-ASPECTS correlated with baseline DWI lesion volume; the relationship with DWI-ASPECTS was somewhat stronger; corresponding median (interquartile range) volumes (mL) were 9 (2–14), 27 (13–42), and 63 (44–68)—(\( P<0.001 \))—for trichotomized DWI-ASPECTS versus 14 (4–28), 21 (8–44), and 44 (20–68)—(\( P=0.043 \))—for CT-ASPECTS.

The AUC for predicting GFO (n=27) was 0.705 (95% CI, 0.57–0.84) for DWI-ASPECTS, 0.58 (95% CI, 0.41–0.68) for CT-ASPECTS, and 0.51 (95% CI, 0.40–0.72) for time interval from stroke onset to procedure start. The AUC difference for DWI-ASPECTS versus CT-ASPECTS was significant (\( P=0.026 \)), whereas the difference between DWI-ASPECTS and time interval from stroke onset to the cath laboratory was not significant (\( P=0.20 \)).

The AUC for predicting DWI volume \( \geq 70 \) (n=5) was 0.912 (95% CI, 0.82–0.99) for DWI-ASPECTS, 0.82 (95% CI, 0.71–0.94) for CT-ASPECTS, and 0.64 (95% CI, 0.41–0.87) for time interval from stroke onset to cath laboratory. The AUC difference for DWI-ASPECTS versus CT-ASPECTS was not significant (\( P=0.31 \)), but the difference between DWI-ASPECTS and time interval from stroke onset to the cath laboratory was significant (\( P=0.032 \); Figure 3).

In this study, inter-rater agreement for CT-ASPECTS was moderate, whereas reader agreement for DWI-ASPECTS was almost perfect. The agreement differences persisted when scores were trichotomized (0–4 versus 5–7 versus 8–10) or dichotomized (0–7 versus 8–10).

DWI-ASPECTS predicted clinical outcome and DWI lesion volume better than CT-ASPECTS. An important limitation of our study is that by design, the CT scans in DEFUSE 2 were obtained before the MRI scans (the median time difference was 1.6 hours). For infarcts that experience growth between the CT and MRI studies, this delay provides a bias in favor of MRI-ASPECTS for predicting outcomes. However, despite this time difference, the mean DWI-ASPECTS scores were not significantly lower than the CT scores (7.6 versus 7.0), and the difference between the scores did not increase in relation to the time difference between CT and MRI. CT scores were just as likely to differ from the MRI scores, irrespective of the time between the scans, and they were not more likely to be higher versus lower than the MRI score. Therefore, a systematic bias toward lower MRI-ASPECTS scores does not account for the superior performance of MRI-ASPECTS.

Accurately determining how much irreversibly injured brain tissue is present has important implication for determining

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**Table 1. Reader Agreement by Modality With Scores Dichotomized (>7 vs ≤7) and Trichotomized ASPECTS (0–4 vs 5–7 vs 8–10) Using Cohen \( \kappa \) Statistic**

<table>
<thead>
<tr>
<th>( \kappa ) Value (95% CI)</th>
<th>( P ) Values to Compare ( \kappa )</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \kappa )</td>
<td>CT vs D WI</td>
</tr>
<tr>
<td>Trichotomized scoring</td>
<td></td>
</tr>
<tr>
<td>Simple ( \kappa )</td>
<td>0.36 (0.18–0.55)</td>
</tr>
<tr>
<td>Weighted ( \kappa )</td>
<td>0.46 (0.28–0.63)</td>
</tr>
<tr>
<td>Dichotomized scoring</td>
<td>0.46 (0.26–0.65)</td>
</tr>
</tbody>
</table>

ASPECTS indicates Alberta Stroke Program Early Computed Tomographic scoring; CI, confidence interval; CT, computed tomography; and DWI, diffusion-weighted MRI.
which patients with stroke are optimal candidates for reperfusion therapy. Historically, a hypodensity of >1/3 of the middle cerebral artery territory on NCCT has been used to exclude patients from many intravenous thrombolysis studies, and recent evidence suggests that large DWI lesions (70–100 mL) are highly predictive of poor outcome after reperfusion.8,15,18 Although using ASPECTS scores improves the use of NCCT for identification of early signs of infarction, NCCT has poor sensitivity for detecting early ischemic changes.19

The superior sensitivity of DWI for detection of early brain ischemia6,20–23 has prompted the comparison of the ASPECTS scores between NCCT and DWI. Two studies, similar in concept to ours, have been published.10,13 In the study by Barber et al,10 delays to imaging and time between modalities were similar to ours, whereas the study by Nezu et al 13 had much shorter onset to imaging time and a smaller difference between CT and MRI acquisition. Whereas the study by Barber et al10 showed no difference in CT-ASPECTS and DWI-ASPECTS agreements, the study by Nezu et al13 (inter-rater agreement for DWI-ASPECTS, \(\rho = 0.818\), was superior to that for CT-ASPECTS, \(\rho = 0.634\)). In contrast to our results, CT-ASPECTS performed well13 or better than 10 DWI-ASPECTS in predicting outcome.

The evaluation of ASPECTS performance is dependent on the frequency and volume of early ischemic change present in the population studied. For example, if most of the patients have high ASPECTS scores, either because of short onset to scan times or milder strokes, readers are more likely to agree on the scores being high, and clinical outcomes will be favorable. Data to support this concept were provided by Weir et al,19 who demonstrated that ASPECTS predicted outcome in a graded fashion (linearly for ASPECTS, 6–10), but it was a poor predictor for lower scores. The frequency of CT-ASPECTS 8

Table 2. Sensitivity and Specificity of Baseline CT-ASPECTS Compared With Baseline DWI-ASPECTS

<table>
<thead>
<tr>
<th>Adjudicated CT-ASPECTS</th>
<th>Adjudicated DWI-ASPECTS</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–7</td>
<td>8–10</td>
<td>Total</td>
</tr>
<tr>
<td>0–7</td>
<td>24</td>
<td>11</td>
</tr>
<tr>
<td>8–10</td>
<td>16</td>
<td>23</td>
</tr>
<tr>
<td>Total</td>
<td>40</td>
<td>34</td>
</tr>
</tbody>
</table>

Using DWI-ASPECTS as the gold standard, performance (95% CI) of CT-ASPECTS: sensitivity, 0.60 (0.43–0.75), specificity, 0.68 (0.49–0.82), positive predictive value, 0.69 (0.51–0.83), and negative predictive value, 0.59 (0.42–0.74). CI indicates confidence interval; CT-ASPECTS, computed tomography Alberta Stroke Program Early Computed Tomographic scoring; and DWI-ASPECTS, diffusion-weighted MRI Alberta Stroke Program Early Computed Tomographic scoring.

Table 3. DWI-ASPECTS Trichotomized Into 8–10, 5–7, and 0–4 Score-Groups Correlated With GFO (\(P=0.004\) for GFO Trend in the Subgroups), Whereas CT-ASPECTS did not (\(P=0.534\))

<table>
<thead>
<tr>
<th>Pairing</th>
<th>DWI-ASPECTS</th>
<th>CT-ASPECTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>8–10 vs 0–4</td>
<td>10.1 (1.2–89)</td>
<td>2.5 (0.3–24.5)</td>
</tr>
<tr>
<td>8–10 vs 5–7</td>
<td>3.1 (1.1–8.9)</td>
<td>1.1 (0.4–2.9)</td>
</tr>
<tr>
<td>5–7 vs 0–4</td>
<td>3.3 (0.4–30)</td>
<td>2.3 (0.2–23.4)</td>
</tr>
<tr>
<td>8–10 vs 0–7</td>
<td>3.9 (1.4–10.6)</td>
<td>1.2 (0.5–3.1)</td>
</tr>
</tbody>
</table>

The table shows ORs of pairwise DWI-ASPECTS and CT-ASPECTS. CI indicates confidence interval; CT-ASPECTS, computed tomography Alberta Stroke Program Early Computed Tomographic scoring; DWI-ASPECTS, diffusion-weighted MRI Alberta Stroke Program Early Computed Tomographic scoring; GFO, good functional outcome; and OR, odds ratio.

Figure 3. Receiver operating characteristic (ROC) curves of DWI-ASPECTS, CT-ASPECTS, and onset to procedure start time for predicting functional outcome (A, modified Rankin Scale [mRS] score, 3–6 and B, DWI volume, \(\geq70\) mL). DWI performed best in predicting both good functional outcome and \(\geq70\) mL DWI volume. CT-ASPECTS indicates computed tomography Alberta Stroke Program Early Computed Tomographic scoring; and DWI-ASPECTS, diffusion-weighted MRI Alberta Stroke Program Early Computed Tomographic scoring.
to 10 was greater in the studies done by Barber et al10 and Nezu et al,13 which may account for the good performance of CT-ASPECTS in those studies.

DWI-ASPECTS scores have been shown to correspond to a wide range of DWI lesion volumes24,25; however, a recent study demonstrated that DWI-ASPECTS ≤ 4 reliably predicted infarct volumes >100 mL and DWI-ASPECTS ≥ 6 reliably predicted volumes <70 mL.26 Therefore, a trichotomized scale may have particular relevance in centers where acute MRI is performed, but software for automated lesion volume calculation is not available.

It is of interest that the time from stroke onset to endovascular therapy was not as robust as the DWI-ASPECTS score for predicting clinical outcomes. In the logistic regression model, age, DWI-ASPECTS, recanalization, target mismatch status, and time since onset were assessed. DWI-ASPECTS was the strongest predictor of outcome (Table I in the online-only Data Supplement). This finding may reflect the variable growth rate of DWI lesions over time, and it implies that the volume of irreversible tissue injury is a more potent predictor of clinical outcome than the time to reperfusion.

There are several limitations of our study. This is a substudy of a larger cohort and includes only the subgroup of patients who had both NCCT and DWI. There were a small number of patients with DWI volumes ≥ 70 in this population. DWI abnormalities may be reversible, but reversal is uncommon and usually involves only a small volume of tissue,15,20 and permanent reversal was rarely seen in DEFUSE 2.27

Conclusions

DWI-ASPECTS demonstrates substantial full-scale, dichotomized, and trichotomized inter-rater agreement, which is superior to CT-ASPECTS. DWI-ASPECTS outperformed CT-ASPECTS in predicting functional outcome and infarct volume in the DEFUSE 2 cohort. DWI-ASPECTS performs particularly well in patient populations where early infarct signs on brain imaging are prevalent.

Sources of Funding

This study was funded by grants from the National Institute for Neurological Disorders and Stroke (R01 NS03932505 [Dr Albers] and K23 NS051372 [Dr Lansberg]) and the Stanford Medical Scholars Fellowship Program.

Disclosures

Dr Albers has equity interest in IschemaView and has worked as a consultant for Coviden, Codman, and Stryker. Dr Jovin is a consultant for Silk Road. The other authors report no conflicts.

References


Supplementary Table I. Logistic regression analysis with DWI-ASPECTS and time to recanalization as predictors for good functional outcome.

<table>
<thead>
<tr>
<th>Variables in the Equation</th>
<th>B</th>
<th>Sig. (p)</th>
<th>OR</th>
<th>95% C.I. for OR</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Lower</td>
</tr>
<tr>
<td>Age</td>
<td>-.097</td>
<td>.003</td>
<td>.907</td>
<td>.850</td>
</tr>
<tr>
<td>Recanalization(^1)</td>
<td>1.757</td>
<td>.337</td>
<td>5.795</td>
<td>.161</td>
</tr>
<tr>
<td>Onset to Procedure End Time</td>
<td>-.090</td>
<td>.548</td>
<td>.914</td>
<td>.680</td>
</tr>
<tr>
<td>Adjudicated DWI-ASPECTS</td>
<td>.583</td>
<td>.023</td>
<td>1.792</td>
<td>1.083</td>
</tr>
<tr>
<td>TMM(^8)</td>
<td>2.086</td>
<td>.122</td>
<td>8.055</td>
<td>.571</td>
</tr>
<tr>
<td>Recanalization by TMM interaction(^9)</td>
<td>-.128</td>
<td>.948</td>
<td>.880</td>
<td>.019</td>
</tr>
<tr>
<td>Constant</td>
<td>-.066</td>
<td>.981</td>
<td>.936</td>
<td></td>
</tr>
</tbody>
</table>

\(^1\)Recanalization = TICI 2b/3. \(^8\)Target Mismatch (TMM) profile included: 1) a ratio between the volumes of critically hypoperfused tissue and the ischemic core \(\geq 1.8\), with an absolute difference \(\geq 15\) mL; 2) ischemic core volume \(< 70\) mL and; 3) volume of tissue with a severe delay in bolus arrival (Tmax\(>10\) sec) \(< 100\) mL. \(^9\)Recanalization by TMM interaction shows if recanalization effect is different in TMM vs. no TMM patients (is p-value significant or not).
Supplementary Figure I. Differences between CT-ASPECTS and DWI-ASPECTS scores did not increase or decrease in relation to the time difference between the two modalities.

None of the time-intervals is different: $p=0.32$ (Kruskal-Wallis test) there is no directional trend: $p=0.31$ (Jonckheere-Terpstra test for ordered alternatives).
CTおよびMRI検査を受けた患者のAlberta Stroke Program Early CT Score（ASPECTS）の読影者間の一致，撮影方法間の一致，および転帰の予測

Alberta Stroke Program Early Computed Tomographic Scoring Performance in a Series of Patients Undergoing Computed Tomography and MRI

Reader Agreement, Modality Agreement, and Outcome Prediction

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表2 追跡開始時にみたDWI-ASPECTSと比較したCT-ASPECTSの感度と特異度

<table>
<thead>
<tr>
<th>積合</th>
<th>判定済み DWI-ASPECTS</th>
<th>判定済み CT-ASPECTS</th>
<th>合計点</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-7</td>
<td>24</td>
<td>8-10</td>
<td>35</td>
</tr>
<tr>
<td>8-10</td>
<td>16</td>
<td>23</td>
<td>39</td>
</tr>
<tr>
<td>合計点</td>
<td>40</td>
<td>34</td>
<td>74</td>
</tr>
</tbody>
</table>

DWI-ASPECTSを判定基準として用いた時のCT-ASPECTSの成績（95%CI）：感度0.60（0.43～0.75）, 特異度0.68（0.49～0.82）, 陽性的中率0.69（0.51～0.83）, および陰性的中率0.69（0.42～0.74）。

CT-ASPECTS：CTによるAlberta Stroke Program Early Computed Tomographic Score, DWI-ASPECTS：拡散強調MRIによるAlberta Stroke Program Early Computed Tomographic Score。

表3 3群（0～4, 5～7, 8～10）に分けたDWI-ASPECTSはGFOと相関したが（サブグループにおけるGFOの傾向：p=0.004), CT-ASPECTSは相関しなかった（p=0.534）

<table>
<thead>
<tr>
<th>積合</th>
<th>DWI-ASPECTS</th>
<th>CT-ASPECTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>8～10 対0～4</td>
<td>10.1 (1.2-89)</td>
<td>2.5 (0.3-24.5)</td>
</tr>
<tr>
<td>8～10 対5～7</td>
<td>3.1 (1.1-8.9)</td>
<td>1.1 (0.4-2.9)</td>
</tr>
<tr>
<td>5～7 対0～4</td>
<td>3.3 (0.4-30)</td>
<td>2.3 (0.2-23.4)</td>
</tr>
<tr>
<td>8～10 対0～7</td>
<td>3.9 (1.4-10.6)</td>
<td>1.2 (0.5-3.1)</td>
</tr>
</tbody>
</table>

DWI-ASPECTSとCT-ASPECTSのORを示す。CI：信頼区間, CT-ASPECTS：CTによるAlberta Stroke Program Early Computed Tomographic Score, DWI-ASPECTS：拡散強調MRIによるAlberta Stroke Program Early Computed Tomographic Score, GFO：良好な機能的転帰, OR：オッズ比。