Higher Incidence of In-Hospital Complications in Patients With Clipped Versus Coiled Ruptured Intracranial Aneurysms

Mervyn D.I. Vergouwen, MD, PhD; Jiming Fang, PhD; Leanne K. Casaubon, MD, MSc, FRCP; Melissa Stamplecoski; Annette Robertson, RN, RDCS; Moira K. Kapral, MD, MSc, FRCP; Frank L. Silver, MD, FRCP; on behalf of the Investigators of the Registry of the Canadian Stroke Network

Background and Purpose—After aneurysmal subarachnoid hemorrhage (SAH), patients with clipped aneurysms have a higher incidence of neurocognitive deficits and seizures compared with patients with coiled aneurysms. It remains unknown if patients with clipped aneurysms also have a higher incidence of other in-hospital complications.

Methods—We used data from the Registry of the Canadian Stroke Network on consecutive patients admitted to hospital with aneurysmal SAH. Patients who died within 2 days after admission were excluded. Baseline characteristics, incidence of various in-hospital complications within 30 days after admission, length of stay, poor functional outcome (modified Rankin Scale score at discharge of ≥3), and mortality were compared between patients with clipped versus coiled aneurysms.

Results—Of the 931 patients, 548 (59%) were clipped and 383 (41%) coiled. Baseline characteristics were similar. Compared with patients with coiled aneurysms, patients with clipped aneurysms had a higher incidence of in-hospital complications (37.2% versus 24.5% of patients; P<0.0001), poor functional outcome at discharge (69.4% versus 51.4%; P<0.0001), mortality (at discharge: 14.6% versus 9.1%; P=0.01), and a longer length of stay (17 [interquartile range, 11 to 29] versus 13 [interquartile range, 7 to 22] days; P<0.0001). Higher incidences were observed for urinary tract infection (P=0.02), pneumonia (P=0.01), cardiac/respiratory arrest (P=0.007), seizure (P=0.01), and decubitus ulcer (P=0.02). Urinary tract infection, pneumonia, cardiac/respiratory arrest, and seizure were independent predictors of poor functional outcome.

Conclusions—Patients with clipped aneurysms have a higher incidence of in-hospital complications than patients with coiled aneurysms, which attributes to a higher risk of poor functional outcome and death and an increased length of stay. (Stroke. 2011;42:00-00.)

Key Words: clipping ■ complications ■ coiling ■ outcome ■ subarachnoid hemorrhage

Aneurysmal subarachnoid hemorrhage (SAH) is a life-threatening disease. Patients who survive the initial hemorrhage have a high risk of long-lasting disability and death, often resulting from complications that occur in the first few weeks after the hemorrhage. Previous studies showed that patients with clipped aneurysms have a higher incidence of neurocognitive deficits and seizures compared with patients with coiled aneurysms. However, it remains unknown if patients with clipped aneurysms also have a higher incidence of other in-hospital complications such as pneumonia or myocardial infarction.

Methods

We used data from Phase 3 of the Registry of the Canadian Stroke Network (RCSN), which is a hospital-based registry of consecutive patients presenting with an acute stroke (ischemic stroke, intracerebral hemorrhage, and subarachnoid hemorrhage) or a transient ischemic attack to 11 regional stroke hospitals in Ontario, Canada. Approval for the RCSN was obtained from the Research and Ethics Board at each of the participating centers. All patients in this registry were identified prospectively and data were abstracted systematically during the hospital stay and after hospital discharge by trained research nurses using a standardized Case Report Form and custom electronic data entry software that increases data quality. For the current analysis, a research protocol with statistical analysis plan was

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Probability value

Aneurysms. Categorical variables were analyzed using the 

Statistical Analyses

Results

Table 1. Baseline Characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>All Patients (N=931)</th>
<th>Neurosurgical Treatment (N=548)</th>
<th>Endovascular Treatment (N=383)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y, mean±SD (no.)</td>
<td>55.4±12.8 (931)</td>
<td>55.0±12.2</td>
<td>56.1±13.6</td>
<td>0.20</td>
</tr>
<tr>
<td>No. of females (%)</td>
<td>635 (68.2%)</td>
<td>369 (67.3%)</td>
<td>266 (69.5%)</td>
<td>0.50</td>
</tr>
<tr>
<td>Hunt &amp; Hess score on admission, median no. (IQR)</td>
<td>2 (2–3)</td>
<td>2 (2–3)</td>
<td>2 (2–3)</td>
<td>0.15</td>
</tr>
<tr>
<td>Charlson comorbidity index ≥2, no./No. (%)</td>
<td>181/926 (19.5)</td>
<td>107/546 (19.6%)</td>
<td>74/380 (19.5%)</td>
<td>0.96</td>
</tr>
<tr>
<td>Systolic blood pressure on admission, mean±SD (no.)</td>
<td>154.0±30.7 (522)</td>
<td>154.0±30.7 (315)</td>
<td>154.0±30.8 (207)</td>
<td>0.98</td>
</tr>
<tr>
<td>Diastolic blood pressure on admission, mean±SD (no.)</td>
<td>83.2±17.0 (520)</td>
<td>83.9±17.5 (314)</td>
<td>82.1±16.2 (206)</td>
<td>0.25</td>
</tr>
<tr>
<td>Glucose level on admission, median (IQR; no.)</td>
<td>7.4 (6.3–8.9; 496)</td>
<td>7.5 (6.3–9.1; 302)</td>
<td>7.35 (6.2–8.7; 194)</td>
<td>0.35</td>
</tr>
</tbody>
</table>

IQR indicates interquartile range; SD, standard deviation.

developed and submitted to the RCSN Publication Committee for approval. We identified all patients admitted to the hospital with aneurysmal SAH between July 1, 2003, and March 31, 2008, who received treatment of the aneurysm either by coiling or clipping. Patients with a final diagnosis of nonstroke, ischemic stroke, or intracerebral hemorrhage were excluded. We also excluded patients with SAH who died within 2 days after admission and those who received both coiling and clip occlusion. Data regarding aneurysm treatment procedures were validated by linking RCSN data to the Canadian Institute for Health Information hospital discharge abstract database (CIHI DAD), in which all procedures during hospitalization are registered. Charlson comorbidity index data were derived from CIHI DAD. RCSN data were linked to the Registered Persons Data Base to investigate 30-day and 90-day overall mortality (both in and out of the hospital).

The following variables were abstracted: (1) baseline characteristics on admission: age, sex, Hunt & Hess score, Charlson comorbidity index, systolic and diastolic blood pressure, and (nonfasting) blood glucose; (2) in-hospital complications that occurred within 30 days after admission: urinary tract infection, pneumonia, sepsis, seizure, deep vein thrombosis, pulmonary embolism, cardiac/respiratory arrest, myocardial infarction, gastrointestinal hemorrhage, decubitus ulcer, and falls with injury; (3) modified Rankin Scale at discharge and death during hospitalization; and (4) 30-day and 90-day overall mortality (both in and out of the hospital).

Definitions

Definitions for each complication were outlined in the RCSN Operations Manual (Online Supplement; http://stroke.ahajournals.org). Only complications that occurred within 30 days after admission were documented in an attempt to avoid including complications that were secondary to long hospitalizations. To be present, a complication had to be documented by imaging and laboratory reports, where appropriate, and confirmed by a physician within the progress notes, consultation reports, or discharge summary. Poor functional outcome was a priori defined as a modified Rankin Scale score of ≥3.

Statistical Analyses

All statistical analyses were performed using a commercially available software package (SAS Version 9.1.3 statistical software; SAS Institute Inc, Cary, NC). Baseline characteristics, incidence of various in-hospital complications, length of stay, poor functional outcome at discharge, and mortality were summarized using descriptive statistics and compared between patients with coiled and clipped aneurysms. Categorical variables were analyzed using the χ² test. A probability value <0.05 was considered statistically significant. Mean values were presented with SD and median values with interquartile range (IQR). No comparisons were made when a cell value was ≤5 to protect the privacy of individuals in the database. A multivariate logistic regression model was used for the outcome parameter “poor functional outcome at discharge.” A Poisson regression method was used for “length of stay.” In the multivariate models, only the 4 most prevalent in-hospital complications were analyzed. Furthermore, no variable selection was applied. Missing Hunt & Hess scale values in 87 patients (9.3% of all patients) were replaced by the median Hunt & Hess scale value. Results of multivariate logistic regression analyses and Poisson regression analyses were presented as ORs and relative risks (RR), respectively, with 95% CIs. We also compared the incidence of various in-hospital complications, length of stay, poor functional outcome at discharge, and mortality in clipped and coiled patients with Hunt & Hess scores 1 to 3 and 4 to 5, respectively. Furthermore, we investigated if there was a change of practice (percentage of coiled patients) over time and if this translated to a change in complications and mortality. For this purpose, we compared 2 timeframes, namely 2003 to 2005 and 2006 to 2008.

Comparison of In-Hospital Complications

The incidence of in-hospital complications is shown in Table 2. Patients with clipped aneurysms had a higher incidence of in-hospital complications than those with coiled aneurysms (37.2% versus 24.5% of patients; P<0.0001). Higher incidences were observed for urinary tract infection (P=0.02), pneumonia (P=0.01), cardiac/respiratory arrest (P=0.007), seizure (P=0.01), and decubitus ulcer (P=0.02), but not for deep vein thrombosis, sepsis, myocardial infarction, gastrointestinal hemorrhage, pulmonary embolism, and fall with injury.

Comparison of Outcome Parameters

Outcome parameters are described in Table 2. Patients with clipped aneurysms had a higher incidence of poor functional outcome at discharge (69.4% versus 51.4% of patients in clipped and coiled patients, respectively; P<0.0001) and mortality (at discharge: 14.6% versus 9.1% in clipped and coiled patients, respectively, P=0.01; 30 days after SAH: 13.9% versus 8.9%, respectively, P=0.02; and 90 days after SAH: 16.1% versus 9.7%, respectively, P=0.005), and a longer median length of stay (17 [IQR, 11 to 29] days in clipped patients versus 13 [IQR, 7 to 22] days in coiled patients; P<0.0001).
Predictors of Poor Functional Outcome

On multivariate analyses, clipping was associated with a higher risk of poor functional outcome (OR, 2.22; 95% CI, 1.61 to 3.08; Figure). The 4 most prevalent complications were independent predictors of poor functional outcome (urinary tract infection: OR, 2.3, 95% CI, 1.3 to 4.0; pneumonia: OR, 3.7, 95% CI, 1.8 to 7.6; cardiac/respiratory arrest: OR, 7.2, 95% CI, 2.0 to 25.7; and seizure: OR, 2.6, 95% CI, 1.1 to 6.0).

Length of Stay

In the entire cohort, the median length of stay was 15 days (IQR, 9 to 26; Table 2). Clipped patients had a longer median length of stay than coiled patients (17 days [IQR, 11 to 29] versus 13 days [IQR, 7 to 22]; P<0.0001). Multivariate generalized linear regression analysis showed that clipping was associated with a longer length of stay compared with coiling (RR, 1.21; 95% CI, 1.18 to 1.25). Urinary tract infection, pneumonia, and seizure were associated with a longer length of stay (RR, 1.69, 95% CI, 1.63 to 1.75; RR, 1.76, 95% CI, 1.70 to 1.82; and RR, 1.28, 95% CI, 1.22 to 1.34, respectively). Cardiac/respiratory arrest was associated with shorter length of stay (RR, 0.87; 95% CI, 0.82 to 0.91).

Comparison of Complications and Outcome in Patients With Clipped and Coiled Aneurysms According to Hunt & Hess Scores

Both in patients with Hunt & Hess score of 1 to 3 and 4 to 5, clipped patients more often had ≥1 complication and poor functional outcome at discharge (Table 3).

Change of Practice Over Time

Over time, we observed a minor increase in percentage of patients being coiled and minor decreases in percentage of patients with at least 1 complication, poor functional outcome, and mortality (Table 4). However, none of these differences reached statistical significance.

Discussion

The results of this large registry-based study show that patients with clipped aneurysms were at increased risk of poor functional outcome and mortality and had a longer length of stay compared with patients with coiled ruptured intracranial aneurysms. These differences in outcome could be attributed to a higher incidence of in-hospital complications in patients with clipped versus coiled aneurysms. The 4 most prevalent complications were urinary tract infection, pneumonia, cardiac/respiratory arrest, and seizure. These 4 complications were all more frequently observed in patients with clipped aneurysms and were independent predictors of poor functional outcome. The effect of clipping on in-hospital complications and functional outcome was not only observed in the subgroup of patients with Hunt & Hess scores 1 to 3, but also in patients with Hunt & Hess scores 4 to 5.

Although other studies have also investigated in-hospital complications in patients with SAH, the current study differs from previous studies.5–8 The current study is the first to compare the incidence of in-hospital complications between clipped and coiled patients. Besides, data were derived from a large, multicenter, regional registry of patients with SAH in...
a large, regional registry. In a single-center study that included 580 patients, it was shown that pneumonia, bloodstream infections, fever, anemia, and hyperglycemia are common after SAH and independently predict poor outcome and death.6,7 Another study included 350 patients with SAH and showed that only high intracranial pressure and neurological deterioration were independently associated with poor outcome.5 A study that included 457 patients with SAH identified the following frequently occurring nonneurological complications: anemia, hypertension, cardiac arrhythmia, fever, electrolyte changes, pulmonary edema, pneumonia, hepatic dysfunction, renal dysfunction, and thrombocytopenia.8 In the latter study, the relationship between individual complications and outcome parameters was not studied.

It remains unknown why clipped patients have a higher incidence of complications such as pneumonia and urinary tract infection than coiled patients. One could argue that these complications were secondary to a longer length of stay in clipped versus coiled patients. To minimize the risk that complications were secondary to a long length of stay, we only included complications that occurred within the first 30 days after admission. Although this still does not rule out that complications were secondary to a prolonged length of stay, it is plausible that the reverse is true, namely, that these complications result in longer length of stays. Because clipped patients had a significantly higher incidence of decubitus ulcer, we hypothesize that clipped patients were bed-bound longer than coiled patients. Prolonged periods of intubation and ventilation result in immobilization, which increases the risk of infections. It can also be hypothesized that clipped patients are at increased risk to develop immunodepression, which increases the risk of infections after

![Figure](Results of multivariate analysis: ORs for having poor functional outcome. The odds ratio for is given for every 10 year increase. * indicates confidence intervals not completely shown: OR 7.2 (95% CI, 2.0–25.7).)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Hunt &amp; Hess Score 1–3</th>
<th>Hunt &amp; Hess Score 4–5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Variable</td>
<td>Clip (N=424)</td>
<td>Coil (N=314)</td>
</tr>
<tr>
<td>≥1 in-hospital complication, no. (%)</td>
<td>132 (31.1)</td>
<td>67 (21.3)</td>
</tr>
<tr>
<td>Median length of stay, d (IQR)</td>
<td>16 (10–25)</td>
<td>12 (7–19)</td>
</tr>
<tr>
<td>Poor outcome at discharge, no./No. (%)</td>
<td>260/422 (61.6)</td>
<td>138/314 (43.9)</td>
</tr>
<tr>
<td>Mortality, no. (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>At discharge</td>
<td>40 (9.4)</td>
<td>22 (7.0)</td>
</tr>
<tr>
<td>30 d after SAH</td>
<td>39 (9.2)</td>
<td>22 (7.0)</td>
</tr>
<tr>
<td>90 d after SAH</td>
<td>45 (10.6)</td>
<td>24 (7.6)</td>
</tr>
</tbody>
</table>

IQR indicates interquartile range; SAH, subarachnoid hemorrhage.
SAH.9 The higher incidence of seizures in clipped patients was also observed in the International Subarachnoid Aneurysm Trial (ISAT) and most likely results from brain damage secondary to craniotomy.2 In our study, cardiac arrest occurred in 6.9% of patients and was strongly associated with poor outcome. In recent years, there is increasing interest in the brain—heart connection.10 It is well known that electrocardiographic abnormalities are common in patients with ischemic stroke, hemorrhagic stroke, and SAH.8,11,12 Abnormalities on electrocardiogram that might lead to cardiac arrest such as QT prolongation are common in patients with stroke.8,11 A recent meta-analysis in patients with SAH showed that markers of cardiac damage and dysfunction are associated with poor outcome and mortality.11 Damage to the insular cortex in patients with stroke has been associated with electrocardiographic abnormalities.8

The results of our study have implications for daily practice. Because clipped patients had a higher incidence of complications including decubitus ulcer, our data suggest that efforts should be done to shorten the period of immobilization. Future studies should focus on the efficacy of strategies that prevent complications. In patients with acute stroke, a meta-analysis of 4 pilot studies showed that prophylactic treatment with antibiotics reduces the incidence of infections.14 No such studies have been done yet in patients with SAH. Patients with SAH with immunodepression might be good candidates to receive prophylactic treatment with antibiotics.9

Several potential limitations need to be addressed. The reported incidence of in-hospital complications can be limited by ascertainment and interobserver bias. Our data are collected by chart review and only complications that are documented in the chart are captured. To improve the reliability of the data, all variables in the RCSN were predefined in the Case Record Form manual and the study nurses were all trained and evaluated by completing standard test charts. Nevertheless, we assume that these potential sources of bias do not account for the observed difference in the incidence of complications between coiled and clipped patients. Second, this was a nonrandomized comparison so that the observed difference in the incidence of complications can result from baseline differences that were not captured in the present analysis. For example, aneurysm location, aneurysm size, and Hiji grade were not captured in this registry. However, we believe that this registry of consecutive patients with SAH represents daily practice. Previously, it was shown that aneurysm location does not affect the incidence of complications.5 We were not able to correct for other covariates that influence outcome parameters such as rebleeding, delayed cerebral ischemia, and hydrocephalus. The latter 3 complications were also not recorded in this registry, which was designed to monitor the process and quality of stroke care in patients with the more prevalent stroke types of ischemic stroke and intracerebral hemorrhage. Because it is still debated if clipping or coiling is associated with an increased risk of delayed cerebral ischemia, this probably does not account for the observed difference in the incidence of complications between clipped and coiled patients.15,16

We conclude that clipping increases the risk of in-hospital complications, which results in an increased length of stay and worse functional outcomes. The most prevalent complications were urinary tract infection, pneumonia, cardiac/respiratory arrest, and seizure. Because we and others found that these complications are independent predictors of poor functional outcome, more aggressive strategies are needed to prevent and treat these complications, especially in clipped patients. In patients with aneurysms that are suitable for both clipping and coiling, endovascular treatment should be the preferred treatment option.

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### Disclosures
None.

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dependency, seizures, rebleeding, subgroups, and aneurysm occlusion. 

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2010;41:2519–2524.
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### Online Supplement S1. Definitions of complications

<table>
<thead>
<tr>
<th>Complication</th>
<th>Definition</th>
<th>Data source</th>
<th>Data entry</th>
</tr>
</thead>
</table>
| Urinary tract infection    | Did the patient have a urinary tract infection within the first 30 days of the hospital stay? | Urine for culture and sensitivity, microbiology report, history and physical, progress notes. Use only physician’s note confirming urinary tract infection. | □ Select “No” if there is no urinary tract infection during the first 30 days of this hospital stay.  
□ Select “Yes” if there is urinary tract infection during the first 30 days of this hospital stay. |
| Pneumonia                  | Did the patient have pneumonia confirmed on X-ray and within the first 30 days of this hospital stay? | Chest X-ray, history and physical, progress notes, consultant’s note. Use only physician’s note confirming pneumonia. | □ Select “No” if there is no pneumonia during the first 30 days of this hospital stay.  
□ Select “Yes” if there is pneumonia during the first 30 days of this hospital stay. |
| Cardiac or respiratory arrest | Did the patient have a cardiac or respiratory arrest within 30 days of admission for this hospital stay?  
(Excluding patients designated by doctor order as DNR) | Resuscitation record, history and physical, progress notes, consultant’s note. Use only physician’s note confirming a cardiac/respiratory arrest. | □ Select “No” if there is no evidence of cardiac/respiratory arrest during this hospital stay.  
□ Select “Yes” if there is evidence of cardiac/respiratory arrest during this hospital stay. |
| Seizure                    | Did the patient demonstrate any kind of seizure activity during the hospital stay? | Progress notes, consultant’s notes, nursing notes | □ Select “No” if the patient showed no evidence of seizure activity.  
□ Select “Yes” if the patient showed evidence of seizure activity. |
| Deep vein thrombosis       | Did the patient develop a deep vein thrombosis within 30 days of admission for this hospital stay? | Nuclear Medicine report, history and physical, nurses’ notes, progress notes, consultant’s note. Use only | □ Select “No” if the patient did not develop a deep vein thrombosis during the first 30 days of this hospital stay.  
□ Select “Yes” if the patient did develop a deep vein thrombosis during the first 30 days of this hospital stay. |
<table>
<thead>
<tr>
<th>Condition</th>
<th>Question</th>
<th>Documentation Sources</th>
<th>Instructions / Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sepsis</td>
<td>Did the patient acquire a septic systemic infection within 30 days of admission for this hospital stay? This variable is designed to capture serious systemic infections other than urinary tract infection or pneumonia, which are captured elsewhere. Examples include “bacteremia”, “peritonitis”, “sepsis”.</td>
<td>Laboratory and imaging tests, history and physical, nurses’ notes, progress notes, consultant’s note. Use only physician’s note confirming sepsis.</td>
<td>Select “No” if the patient did not acquire a septic infection within 30 days of admission for this hospital stay. Select “Yes” if the patient did acquire a septic infection within 30 days of admission. Select “UTD” if there is not sufficient documentation to determine if there was a sepsis during the first 30 days of admission.</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>Did the patient have a myocardial infarction after arrival and within the first 30 days of this hospital stay?</td>
<td>E.C.G., history and physical, progress notes, consultant’s note. Use only physician’s note confirming myocardial infarction.</td>
<td>Select “No” if there is no evidence of myocardial infarction during the first 30 days of this hospital stay. Select “Yes” if there is evidence of myocardial infarction during the first 30 days of this hospital stay.</td>
</tr>
<tr>
<td>Gastro-intestinal hemorrhage</td>
<td>Did the patient develop a gastro-intestinal hemorrhage within 30 days of admission for this hospital stay?</td>
<td>Laboratory and imaging tests, history and physical, nurses’ notes, progress notes, consultant’s note. Use only physician’s note confirming gastro-intestinal hemorrhage.</td>
<td>Select “No” if the patient did not develop a gastro-intestinal hemorrhage within 30 days of admission for this hospital stay. Select “Yes” if the patient did develop a gastro-intestinal hemorrhage within 30 days of admission. Select “UTD” if there is not sufficient documentation to determine if there was a gastro-intestinal hemorrhage during the first 30 days of admission.</td>
</tr>
<tr>
<td>Condition</td>
<td>Question</td>
<td>Document Sources</td>
<td>Instructions</td>
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| **Decubitus ulcer**        | Did the patient develop a decubitus ulcer within 30 days of admission?   | History and physical, nurses’ notes, progress notes, consultant’s note. Use only physician’s or nurses’ note confirming decubitus ulcer. | □ Select “No” if the patient did not develop a decubitus ulcer during the first 30 days of this hospital stay.  
□ Select “Yes” if the patient did develop a decubitus ulcer during the first 30 days of this hospital stay. |
| **Pulmonary embolism**     | Did the patient develop a pulmonary embolus within 30 days of admission? | Nuclear Medicine report, history and physical, nurses’ notes, progress notes, consultant’s note. Use only physician’s note confirming pulmonary embolus. | □ Select “No” if the patient did not develop a pulmonary embolus during the first 30 days of this hospital stay.  
□ Select “Yes” if the patient did develop a pulmonary embolus during the first 30 days of this hospital stay. |
| **Fall with injury**       | Did the patient fall and fracture or severely injure him/herself within 30 days of admission? | X-ray, history and physical, nurses’ notes, progress notes, consultant’s note. Use only physician’s note confirming injury. | □ Select “No” if the patient did not fall and fracture or severely injure him/herself within 30 days of admission for this hospital stay.  
□ Select “Yes” if the patient did fall and fracture or severely injure him/herself within 30 days of admission.  
□ Select “UTD” if there is not sufficient documentation to determine if there was an injury. |

Legends: DNR = do not resuscitate; UTD = unable to determine