Ventriculostomy is one of the most commonly performed acute neurosurgical procedures. According to the National Neurosurgical Procedural Statistics published by the American Association of Neurological Surgeons, over 42,000 external ventricular drains (EVDs) were placed in 2006. Furthermore, there has been a significant increase in the frequency of EVD placement over the past decade. Given the high prevalence of ventriculostomy, it is critical to systematically characterize the risks associated with this procedure.

Although ventriculostomy is generally considered a safe and efficacious tool for diagnosing and treating increased intracranial pressure (ICP), there are known risks associated with this intervention. The most common complications are infection and hemorrhage; however, reported rates of these complications in the literature are typically low enough to justify the use of an EVD as a standard of care in patients with elevated ICP. A number of recent studies have suggested that the rate of hemorrhage following EVD placement may actually be higher than previously reported. In fact, Maniker et al. documented a 33% rate of postventriculostomy hemorrhage, with rates as high as 39% in patients with a cerebrovascular indication for ventriculostomy.

The aims of the present study were two-fold: We sought, first, to determine the incidence of postventriculostomy hemorrhage in a cohort of patients with intracerebral hemorrhage (ICH) and to identify predictors of hemorrhagic complications of EVD placement.
primary diagnosis of intracerebral hemorrhage (ICH) and, second, to identify patient characteristics that may be predictive of EVD-related hemorrhage in the ICH patient population.

Methods

Study Subjects

All patients 18 years of age and older presenting to Columbia University Medical Center between January 2010 and December 2012 with a primary diagnosis of spontaneous ICH were eligible for the present study. Of the 271 patients who presented with ICH during this time period, 74 (27.3%) underwent placement of an EVD. Demographics, patient characteristics, medical history, and medical and radiographic data were collected prospectively. This study is a post hoc analysis of prospectively collected data. The Columbia University Institutional Review Board approved this study.

Insertion of the EVD and Neurological Evaluation

Columbia University neurosurgical house staff performed all ventriculostomy procedures at bedside in the neurological intensive care unit. The standard of care was to use a Venticlear II catheter (Medtronic), which has an outer diameter of 3.0 mm. In the subset of patients with intraventricular hemorrhage and casting of at least one ventricle, a larger-diameter “trauma” catheter with an outer diameter of 4.9 mm was used. In 71 (95.9%) of 74 patients, frontal access was selected, utilizing Kocher’s point as the target entry site. Hair in the frontoparietal region of the side of interest was shaved using a clipper, and the surgical site was prepared with Betadine and chlorhexadine. The location of Kocher’s point was determined by measuring 12 cm posteriorly from the glabella and 3 cm laterally from the midline. A 1- to 2-cm incision was made down to the bone, and a bur hole was created in an orthogonal plane to the outer table of the skull. An 18-gauge needle was used to perform a durotomy, and the EVD catheter and stylet were then passed into the ventricle with a trajectory aimed at the foramen of Monro, utilizing the ipsilateral epicranus and the external acoustic meatus as landmarks. After traversing the ependyma at 3–4 cm, the stylet was removed and the catheter passed to a depth of 6–7 cm from the outer lamina of the skull. The proximal catheter was then tunneled 2–3 cm in a postero-medial direction and secured with 2-0 silk sutures.

Throughout each patient’s stay in the neurological intensive care unit, an attending neurosurgeon or neurosurgeon performed neurological examinations at least twice daily. Neurological deterioration was defined as a decline in the Glasgow Coma Scale (GCS) score of 2 or more points for at least 24 hours. Postventriculostomy hemorrhages were considered to be clinically significant when EVD placement coincided with neurological deterioration. Functional outcome was assessed using the modified Rankin Scale (mRS) at the time of hospital discharge (or at 14 days after ICH onset, whichever occurred first) and then again at 90 ± 14 days. At each time point, patients were stratified according to functional outcome (good functional outcome if the mRS score was ≤ 3, poor functional outcome if the mRS score was ≥ 4) and according to mortality.

Radiographic Imaging and Analysis

Radiographic imaging was performed according to the standard clinical protocol, which includes pre- and postprocedural noncontrast head CT scans; no additional scans were obtained solely for the purpose of this study. Only those patients with both pre- and postprocedural imaging were included in the study. Of the 74 patients who underwent ventriculostomy, 5 did not have preoperative imaging available for analysis. Each of these 5 patients had undergone preprocedural imaging at an outside hospital prior to being transferred to the Columbia University Medical Center; therefore, the images were not available for review on Columbia’s electronic medical records.

All CT images were obtained on a 16-slice multidetector CT scanner (LightSpeed RT16, GE Healthcare). Two independent medical professionals, who were blinded to the clinical data, reviewed all head CT scans with 100% interobserver reliability. The area within and immediately adjacent to the EVD catheter tract was scrutinized for hyperdense lesions that were not visible on preoperative imaging. In cases in which the etiology of the hyperdense lesion was uncertain, Hounsfield units were measured to confirm the presence of hemorrhage; any lesion with between 40 and 80 HU was considered to be consistent with acute blood.

Statistical Analysis

Statistical analyses were performed with SAS 9.3 (SAS Institute Inc.). Univariate analyses were performed to identify predictors of postventriculostomy hemorrhage. Analyzed variables included relevant patient characteristics, medical history, clinical presentation, laboratory studies, and interventions. The Student t-test, Wilcoxon rank-sum test, Fisher’s exact test, Pearson’s χ² test, and simple logistic regression were used, as appropriate. All variables with a p < 0.20 were included in a stepwise multiple logistic regression model to identify independent predictors of postventriculostomy hemorrhage.

Results

Sixty-nine patients had both pre- and postprocedural imaging and were included in this analysis. The average age of these patients was 58.9 ± 16.0 years. As described above, frontal access was used for EVD placement in 71 (95.9%) of 74 of the patients. Occipital access was used for the remaining 3 patients (4.1%); the primary ICH was cerebellar in all 3 of these patients. The time between preprocedural imaging and EVD insertion was 3.85 ± 3.26 hours, and the time between EVD insertion and postprocedural imaging was 1.67 ± 0.70 hours. The time between preprocedural blood pressure measurement and the subsequent procedure was 1.2 ± 1.3 hours.

Of the 69 patients, 22 (31.9%) had postventriculostomy hemorrhage. Intraparenchymal hemorrhage occurred in 19 (86.4%) of these 22 patients, subarachnoid hemor-
Postventriculostomy hemorrhage

harge in 3 (13.6%), subdural hemorrhage in 1 (4.5%), and epidural hemorrhage in 1 (4.5%); 1 patient experienced simultaneous intraparenchymal and subdural hemorrhages, and 1 patient had both intraparenchymal and subarachnoid hemorrhages. The majority of bleeds were small and subclinical. Among all patients with intraparenchymal hemorrhage, the mean hemorrhage volume was $0.66 \pm 1.06 \text{ cm}^3$. Stratified according to ventricular catheter diameter, patients treated with smaller-diameter (3.0 mm) catheters had a significantly greater mean hemorrhage volume than patients treated with larger-diameter (4.9 mm) catheters (0.84 ± 1.2 cm$^3$ vs 0.14 ± 0.12 cm$^3$, $p = 0.049$). Postventriculostomy hemorrhage was clinically significant in only 1 patient (1.4%); the location of the bleed in this patient was epidural.

The variables that met the criteria for inclusion in the multivariate model were an age > 75 years, admission GCS score < 9, international normalized ratio (INR) > 1.16, and factor VII transfusion (Table 1). Since no patients in the EVD-related hemorrhage group received a factor VII transfusion, this variable was excluded from the multiple logistic regression analysis. In the final multivariate model, only age > 75 years was an independent predictor of postventriculostomy hemorrhage (OR 7.459 [1.565–35.554], $p = 0.01$; Table 2).

Functional outcome data were available for 100% of the patients at the time of hospital discharge or at 14 days after ICH onset and for 61 (88.4%) of 69 patients at the 90-day follow-up. Poor functional outcome occurred in 62 (89.9%) of 69 patients at discharge and in 44 (72.1%) of 61 patients at 90 days. Mortality rate was 29.0% (20 of 69 patients) at discharge and 54.1% (33 of 61 patients) at 90 days. Among patients who suffered postventriculostomy hemorrhage, there was no statistically significant difference in the rate of poor functional outcome or of mortality at either time point (Table 3).

### Discussion

Ventriculostomy is a commonly performed procedure for patients with acute neurological injury. Reported rates of postventriculostomy hemorrhage vary significantly in the literature; however, most studies are limited by inconsistent imaging protocols and heterogeneous patient populations with disparate indications for EVD insertion. A recent study by Maniker et al., which included only patients with both pre- and postventriculostomy imaging data, documented hemorrhage rates as high as 33% following EVD insertion. In addition, these authors stratified patients according to admitting diagnosis and found an even higher rate of hemorrhage in patients with a cerebrovascular indication for EVD placement. In the present study, we sought to confirm this significant rate of postventriculostomy hemorrhage in a cohort of patients with ICH. Furthermore, we sought to investigate the risk factors for EVD-related hemorrhage in this patient population. Although a number of prior studies have evaluated risk factors for EVD-related hemorrhage, these analyses were retrospective and included only a limited number of variables. The present study is the first in which predictors of postventriculostomy hemorrhage are prospectively and comprehensively evaluated.

The incidence of hemorrhagic complications of EVD placement in our ICH cohort was 31.9%. This rate is sig-

### TABLE 1: Univariate analyses of postventriculostomy hemorrhage*

<table>
<thead>
<tr>
<th>Parameter</th>
<th>All Patients</th>
<th>Postventriculostomy Hemorrhage</th>
<th>No Postventriculostomy Hemorrhage</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>no. of patients</td>
<td>69</td>
<td>22</td>
<td>47</td>
<td></td>
</tr>
<tr>
<td>age &gt;75 yrs</td>
<td>15.9%</td>
<td>31.8%</td>
<td>8.5%</td>
<td>0.01</td>
</tr>
<tr>
<td>male sex</td>
<td>60.9%</td>
<td>68.2%</td>
<td>57.5%</td>
<td>0.39</td>
</tr>
<tr>
<td>white race</td>
<td>24.6%</td>
<td>22.7%</td>
<td>25.5%</td>
<td>0.80</td>
</tr>
<tr>
<td>admission GCS score &lt;9</td>
<td>60.9%</td>
<td>72.7%</td>
<td>55.3%</td>
<td>0.17</td>
</tr>
<tr>
<td>creatinine &gt;1.7</td>
<td>16.4%</td>
<td>20.0%</td>
<td>14.9%</td>
<td>0.61</td>
</tr>
<tr>
<td>INR &gt;1.16</td>
<td>28.6%</td>
<td>15.8%</td>
<td>34.1%</td>
<td>0.14</td>
</tr>
<tr>
<td>platelet count (per ml blood)</td>
<td>233.8 ± 81.4</td>
<td>223.8 ± 96.3</td>
<td>238.0 ± 75.0</td>
<td>0.56</td>
</tr>
<tr>
<td>MAP (mm Hg)</td>
<td>92.5 ± 19.2</td>
<td>88.2 ± 16.7</td>
<td>94.8 ± 20.3</td>
<td>0.27</td>
</tr>
<tr>
<td>oral anticoagulants</td>
<td>13.0%</td>
<td>9.1%</td>
<td>14.9%</td>
<td>0.50</td>
</tr>
<tr>
<td>antiplatelet therapy</td>
<td>33.3%</td>
<td>31.8%</td>
<td>34.0%</td>
<td>0.86</td>
</tr>
<tr>
<td>platelet transfusion</td>
<td>53.6%</td>
<td>59.1%</td>
<td>51.1%</td>
<td>0.53</td>
</tr>
<tr>
<td>FFP transfusion</td>
<td>17.4%</td>
<td>13.6%</td>
<td>19.2%</td>
<td>0.57</td>
</tr>
<tr>
<td>factor VII transfusion</td>
<td>5.8%</td>
<td>0.0%</td>
<td>8.5%</td>
<td>0.16</td>
</tr>
<tr>
<td>APACHE II</td>
<td>17.6 ± 8.3</td>
<td>19.1 ± 7.1</td>
<td>16.9 ± 8.7</td>
<td>0.26</td>
</tr>
<tr>
<td>smoking history</td>
<td>44.9%</td>
<td>54.6%</td>
<td>40.4%</td>
<td>0.27</td>
</tr>
<tr>
<td>lobar location of hemorrhage</td>
<td>19.4%</td>
<td>23.8%</td>
<td>17.4%</td>
<td>0.54</td>
</tr>
<tr>
<td>catheter diameter 4.9 mm</td>
<td>20.3%</td>
<td>22.7%</td>
<td>19.2%</td>
<td>0.76</td>
</tr>
</tbody>
</table>

* Values are expressed as the mean ± standard deviation or as a percentage. APACHE II = acute physiology and chronic health evaluation score; FFP = fresh-frozen plasma; MAP = mean arterial pressure.
significantly higher than the rate of hemorrhage reported in many of the earlier series of patients undergoing ventriculostomy and more consistent with those in some more recent studies, including those by Maniker et al. (33%) and Gardner et al. (41%). There is no doubt that advancements in imaging technology have facilitated the detection of small hemorrhages that were previously undetectable. Therefore, it is not surprising that the highest rates of postventriculostomy hemorrhage (41%, 33%, and 18%) in the literature were reported in 2009, 2006, and 2008 (respectively), whereas older studies consistently documented hemorrhage rates less than 2%. Furthermore, in the present study—and in other studies with similarly high rates of hemorrhage—postventriculostomy imaging was consistently performed and carefully scrutinized for evidence of acute hemorrhage. In contrast, many of the earlier studies relied on radiology reports from inconsistent postprocedural imaging, and therefore subtle hemorrhages may have been overlooked. This explanation is supported by a 2009 meta-analysis of hemorrhagic complications of ventriculostomy, in which the authors reported a hemorrhage rate of 10.1% in the studies in which routine CT scanning post–EVD placement was performed versus a rate of 1.5% when routine CT was not performed. Furthermore, the rate of clinically significant postventriculostomy hemorrhage has been relatively constant throughout the literature; the rate of clinically significant hemorrhage in our ICH cohort (1.4%) is consistent with previous reports.

As stated above, a number of prior studies have evaluated the impact of certain risk factors on the incidence of postventriculostomy hemorrhage. Specifically, it has been reported that the setting of EVD placement (bedside vs operating room), INR, and cranial access site (Kocher’s point vs forehead) are not predictive of hemorrhage, whereas dual antiplatelet therapy has been associated with an increased risk. In addition, Maniker et al. noted that admitting diagnosis is a predictor of postventriculostomy hemorrhage, but that age, sex, and catheter diameter are not predictive. In the present study, we evaluated the impact of several different variables on the incidence of hemorrhagic complications of EVD insertion (Table 1). The only variable found to be independently predictive of postventriculostomy hemorrhage was an age > 75 years. There was a trend toward an increased rate of hemorrhage in patients with a severely depressed neurological status at presentation (defined as GCS score < 9); however, this trend did not reach statistical significance in either the univariate or the multivariate analysis. Interestingly, a supra-normal INR (> 1.16) at admission was significantly more common in patients who did not experience postprocedural hemorrhage; this paradoxical finding may be explained by the fact that patients with abnormal coagulation parameters at baseline were significantly more likely to receive a fresh-frozen plasma transfusion (44.4% vs 4.4%, p < 0.0001) or factor VII transfusion (16.7% vs 0%, p < 0.01) than were patients with normal coagulation studies at presentation. Perhaps not surprisingly, patients who experienced hemorrhage after EVD placement were less likely to have received a factor VII transfusion (0% vs 8.5% in patients without EVD-related hemorrhage), but this difference did not reach statistical significance. It is important to note that this variable was not included in the final multivariate model despite having a p < 0.20 in the univariate analysis. The reason for this omission is that postventriculostomy hemorrhage occurred in no patients who had received a factor VII transfusion, and therefore inclusion of this variable in the multiple logistic regression model would lead to inaccurate inflation of the confidence interval; that is, the exponentiated coefficient

<table>
<thead>
<tr>
<th>Parameter</th>
<th>OR</th>
<th>95% CI</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>age &gt;75 yrs</td>
<td>7.46</td>
<td>1.57–35.55</td>
<td>0.01</td>
</tr>
<tr>
<td>admission GCS score &lt;9</td>
<td>2.36</td>
<td>0.62–9.00</td>
<td>0.21</td>
</tr>
<tr>
<td>INR &gt;1.16</td>
<td>0.27</td>
<td>0.06–1.29</td>
<td>0.10</td>
</tr>
</tbody>
</table>

Variables included in this model met the criterion of p < 0.2 in a univariate regression analysis.

### Table 2: Summary of functional outcome data in 69 patients who underwent EVD placement

<table>
<thead>
<tr>
<th>Parameter</th>
<th>All Patients</th>
<th>Postventriculostomy Hemorrhage</th>
<th>No Postventriculostomy Hemorrhage</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>total no. of patients</td>
<td>69</td>
<td>22</td>
<td>47</td>
<td></td>
</tr>
<tr>
<td>discharge poor functional outcome</td>
<td>89.9%</td>
<td>90.9%</td>
<td>89.4%</td>
<td>0.63</td>
</tr>
<tr>
<td>mortality</td>
<td>28.9%</td>
<td>22.7%</td>
<td>31.9%</td>
<td>0.43</td>
</tr>
<tr>
<td>90 days† poor functional outcome</td>
<td>72.1%</td>
<td>75.0%</td>
<td>70.7%</td>
<td>0.73</td>
</tr>
<tr>
<td>mortality</td>
<td>54.1%</td>
<td>60.0%</td>
<td>51.2%</td>
<td>0.52</td>
</tr>
</tbody>
</table>

* Poor functional outcome = mRS score ≥ 4.
† Data available for 61 patients.
would be undefined. Larger studies are therefore necessary to more accurately assess the impact of factor VII transfusion on the risk of EVD-related hemorrhage.

The consideration of catheter gauge as a potential predictor of hemorrhage is based on prior results reported by Maniker et al., specifically, that hemorrhage volume was significantly greater in patients treated with smaller-diameter catheters (2.5 mm) than in those treated with larger-diameter catheters (3.0 mm). This finding was hypothesized to be a false-positive, as there is no plausible biological rationale for this finding.18 Interestingly, we found a similar association between smaller catheter diameter (3.0 vs 4.9 mm) and larger hemorrhage volume (p = 0.049). One possible explanation for this seemingly paradoxical finding is that the larger-diameter catheters may exert greater outward radial pressure, which may tamponade hemorrhage from any vessels damaged during catheter insertion. Further investigation is warranted to validate this hypothesis.

As mentioned above, a cerebrovascular indication for EVD placement has been associated with a greater incidence of hemorrhage. It has been hypothesized that an increased incidence of hypertension in patients with acute cerebrovascular injury, as compared with that in patients with other indications for EVD insertion, may underlie this greater incidence of hemorrhage.19 In the present study, mean arterial pressure immediately prior to EVD insertion was not significantly different in patients who did versus those who did not experience postventriculostomy hemorrhage. Neither were systolic or diastolic pressures significantly different between these two cohorts (data not shown). This finding suggests that elevated blood pressure may not be the mechanism underlying the increased rate of hemorrhagic complications in patients with a cerebrovascular indication for ventriculostomy. An alternative explanation is that these patients may have greater vessel fragility by nature of their underlying susceptibility to cerebrovascular injury. This hypothesis is supported by the fact that an advanced age is the only independent predictor of EVD-associated hemorrhage in our ICH cohort. Pathological studies of blood vessels from patients with hemorrhagic stroke have revealed greater than expected intimal fibrosis, medial degeneration, and atherosclerosis; these pathological changes also occur at an accelerated rate in the blood vessels of elderly subjects.26 Thus, the mechanisms underlying the increased incidence of postventriculostomy hemorrhage in patients with cerebrovascular injury may be similar to the pathophysiology of age-related increases in vascular fragility.

Functional outcome assessment at hospital discharge and at 90 days after ICH onset revealed no significant increase in the rates of poor functional outcome or death in those patients who suffered from hemorrhagic complications of EVD placement. This finding is not particularly surprising given the small average volume of postventriculostomy hematomas. Yet, although the majority of hemorrhagic complications of ventriculostomy are small and ostensibly subclinical, there is, nonetheless, a substantial rationale for taking measures to prevent such hemorrhages. It is important to recognize that the particular definition used to classify a hemorrhage as clinically significant in any given study is not necessarily sensitive to subtle neurological deficits. Furthermore, it is inevitable that when grading neurological function as a discrete variable, there will be some threshold level of neurological function above which the hemorrhage is classified as clinically insignificant, despite the presence of perceptible deficits. Interestingly, a 2003 diffusion-weighted imaging study of ICH demonstrated ischemic damage to brain parenchyma that extends beyond the margins of the hematoma. Thus, even when a hemorrhage does not manifest with acute neurological deficits, there may be unrecognized clinical consequences, and thus every effort should be made to minimize the occurrence of EVD-associated hemorrhage.

We recognize the limitations of this study. It is a single-center study with a relatively small sample size (69 patients), and therefore the multivariate analysis may not be adequately powered to identify all predictors of postventriculostomy hemorrhage. Since we investigated the hemorrhagic complications of EVD placement specifically in patients with ICH, the reported results are not necessarily generalizable to patients undergoing ventriculostomy for other indications. In addition, there are certainly some variables that may contribute to EVD-associated hemorrhage that were not considered in our study, including the number of passes with the ventricular catheter, the skill and experience of the operator, and the degree of inflammatory infiltrate in surrounding brain parenchyma; these variables should be examined in future studies. Future investigation of hemorrhagic complications of ventriculostomy should also strive for larger sample sizes composed of patients with multiple different indications for EVD insertion. Finally, additional studies are warranted to further characterize the clinical consequences of small hemorrhagic complications of EVD placement.

Conclusions
Hemorrhagic complications occur in a substantial percentage of patients with ICH who have undergone ventriculostomy, although these bleeds tend to be small and largely subclinical. In this cohort of ICH patients, an age > 75 years independently predicted EVD-associated hemorrhage. Additional studies are warranted to further explore the risk factors and mechanisms associated with postventriculostomy hemorrhage.

Disclosure
The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.
Author contributions to the study and manuscript preparation include the following. Conception and design: Connolly, Sussman, Kellner, RA Bruce. Acquisition of data: Sussman, Kellner, Nelson, RA Bruce. Analysis and interpretation of data: Connolly, Sussman, Kellner, McDowell, SS Bruce, RA Bruce, Zhuang. Drafting the article: Sussman, Kellner. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Statistical analysis: Sussman, Kellner, McDowell, SS Bruce.

References
1. American Association of Neurological Surgeons: National


Accepted December 3, 2013.
Please include this information when citing this paper: published online January 10, 2014; DOI: 10.3171/2013.12.JNS131685.
Address correspondence to: E. Sander Connolly, M.D., Department of Neurological Surgery, 710 W. 168th St., New York, NY 10032. email: esc5@columbia.edu.