Risk Factors for Traumatic and Bloody Lumbar Puncture in Children With Acute Lymphoblastic Leukemia

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Although lumbar puncture (LP) is generally safe, there is a risk of traumatic LP.1-6 When LPs are difficult to perform or repeated attempts are necessary, blood can be introduced into the cerebrospinal fluid (CSF). Although the mechanism of bleeding into the CSF at the time of LP is not known with certainty, overinsertion of the needle, leading to laceration of the vertebral venous plexus as the needle hits the vertebral body, is a likely cause.7 In extreme cases, overinsertion of the LP needle can lead to CSF contamination with bone marrow and blood.8 Even when the depth of needle insertion is appropriate, the CSF can be contaminated with blood, and in such cases, the source may be the small radicular vessels along the nerve roots at the level of the LP.9 If the patient moves during the procedure, additional soft tissues may be traumatized, leading to bloody CSF.

Blood in the CSF alters the cell count, increases the protein level, and can cause false-positive culture and cytologic results, with consequent diagnos-

See also Patient Page.

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tic confusion.\textsuperscript{5,10-15} Furthermore, bacteria\textsuperscript{16-28} or leukemic cells\textsuperscript{27} circulating in blood may be introduced into the CSF as a result of traumatic LP, thereby worsening the patient’s prognosis. Traumatic or bloody LPs have been defined as those in which the CSF contains more than 200, 500, or 1000 red blood cells (RBCs) per microliter.\textsuperscript{5,13-15,28,29} Reported incidences range from 8% to 19%, depending on the population studied and the definition used.\textsuperscript{19,30-31} Risk factors for traumatic and bloody LP have not been systematically identified.

Patients with acute lymphoblastic leukemia (ALL) undergo multiple LPs to assess central nervous system involvement and to instill intrathecal chemotherapy and are frequently thrombocytopenic. Hence, this population is an excellent group in which to study the effects of thrombocytopenia and repeated procedures on the risk of traumatic and bloody LP. We reviewed the outcomes of LPs performed on pediatric patients with ALL treated at St Jude Children’s Research Hospital, Memphis, Tenn, and identified both unmodifiable and modifiable risk factors for traumatic and bloody LP. The risk of neurologic complications of LP in thrombocytopenic patients with childhood ALL, such as spinal hematoma, has been examined elsewhere.\textsuperscript{32}

**METHODS**

**Patients and Procedures**

Nine hundred fifty-eight pediatric patients with newly diagnosed ALL were treated on 4 consecutive protocols\textsuperscript{33} between February 1984 and July 1998, for which informed consent was obtained from parents or the patient, if 18 years or older. Induction chemotherapy included prednisone, 1-asparaginase, vincristine sulfate, daunorubicin hydrochloride, etoposide (or teniposide), and cytarabine, with or without methotrexate. In addition to diagnostic LP, patients underwent 2 to 12 (median, 4) LPs within 6 months of diagnosis for the administration of intrathecal chemotherapy. For each LP, the patient’s platelet count, the number of RBCs per µL of CSF, and whether platelet transfusion was given were recorded. The institutional review board approved the study.

**Exclusion Criteria and Evaluable Procedures**

Of the 958 children treated for ALL during the review period, 2 were excluded, one because of early death before LP and the other because of intracranial hemorrhage at diagnosis with grossly bloody CSF with all LPs, which were performed to relieve pressure. The remaining 956 patients underwent 5625 LPs; 16 were excluded because no CSF results were documented. An additional 103 LPs were excluded from analyses that required a platelet count because either no platelet count was determined within 1 day of LP (n=58) or no platelet count was documented after platelet transfusion (n=45). Therefore, 956 patients underwent 5609 evaluable LPs, of which 5506 were associated with an evaluable platelet count.

**Definition of Traumatic LP and Bloody LP**

We defined traumatic LPs as those in which the CSF contained at least 10 RBCs per microliter because this degree of blood contamination of CSF is associated with a worsened prognosis in pediatric patients with ALL and circulating lymphoblasts.\textsuperscript{27} We defined bloody LPs as those in which the CSF contained at least 500 RBCs per microliter; this degree of blood contamination causes diagnostic confusion for patients with suspected meningitis\textsuperscript{13,15} and possibly increased risk of introducing bacteria into the CSF when LP is performed on patients with bacteremia.\textsuperscript{22-25} By these definitions, bloody LP is a subset of traumatic LP.

**Specification of Variables and Statistical Analysis**

Age, race, sex, treatment era, treatment protocol, recent use of glucocorticoid or 1-asparaginase, platelet count at LP, number of days since the previous LP, practitioner experience level, the traumatic or bloody status of the previous LP, and the platelet count at the previous LP were considered possible risk factors for traumatic and bloody LP. Age categories were younger than 1 year and 1 to 18 years because of the obvious differences in the unadjusted risk of study outcomes below and above the age of 1 year. Treatment era was divided into an early period (February 1984 to April 1995) and a recent period (May 1995 to July 1998). During the early period, LPs were usually performed on patients in the inpatient ward or outpatient clinic without sedation or under conscious sedation with meperidine hydrochloride and pentobarbital sodium; during the recent period, LPs were generally performed on patients under general anesthesia with propofol in a special procedure area with an anesthesiologist and dedicated staff. The effects of the ALL protocol and recent administration of glucocorticoids or 1-asparaginase were also analyzed. Recent use of glucocorticoid or 1-asparaginase was defined as any administration of the drug within 7 days before the LP and was categorized into 4 groups: neither drug, only glucocorticoid, only 1-asparaginase, or both drugs administered. Because use of these drugs produces a hypercoagulable state, we hypothesized that the risk of traumatic and bloody LP would be decreased if performed after administration of glucocorticoid, 1-asparaginase, or both.

The categories for time since the previous LP were 1 day, 2 to 3 days, 4 to 7 days, 8 to 15 days, and 16 days or more. Practitioners were categorized according to the number of LPs they performed in this cohort of patients with ALL (≤10, 11-50, 51-200, and >200 per practitioner). There were 230 practitioners in the least experienced group (category 1), 70 in category 2, 13 in category 3, and 7 in the most experienced group (category 4). The effect of education level (attending physician, nurse practitioner, fellow, resident) was evaluated in preliminary analyses. Attending physicians and nurse practitioners, who performed 3519 of the 5484 LPs with evaluable practitioner information, had a lower proportion of traumatic LPs.
Traumatic or bloody LP than fellows or residents in univariate analysis, but when experience category was added to the model, the effect of education disappeared, and therefore only the results for experience category are reported. Platelet counts from 1×10^3/µL to 100×10^3/µL were categorized in increments of 25×10^3/µL. Platelet counts higher than 100×10^3/µL comprised a single category because bleeding time and other measures of hemostasis are normal when the platelet count is above this value.34,35 The platelet count at the previous LP was considered a possible risk factor because thrombocytopenia at the previous procedure may allow persistent leakage of blood into the CSF that would be present at the subsequent LP. Platelet counts from the previous LP were categorized in the same way as platelet counts measured at the current LP.

We modeled the risk of traumatic and bloody LP by using logistic regression and included 2 types of intrapatient correlations: a longitudinal correlation and an exchangeable covariance structure that accounted for unmeasured intrapatient factors. The longitudinal correlation was modeled as a first-order Markov chain36 by including the previous LP status as a predictor variable. The model was fit by using generalized estimating equations according to the method of Liang and Zeger37 as implemented by SAS statistical software version 8 (SAS Institute Inc, Cary, NC). Because the purpose of this study was to identify risk factors rather than to test a particular hypothesis, we report odds ratios (ORs) with 95% confidence intervals (CIs). Odds ratios whose 95% CIs do not include 1.0 are associated with P<.05. All reported ORs resulted from multiple logistic regression using the risk factors as predictor variables and the exchangeable within-patient covariance structure as input to the GENMOD procedure in the SAS statistical program.

**RESULTS**

The 523 male patients (55%) and 433 female patients (45%) ranged in age from 1 month to 18 years (median, 5.5 years), 775 (81%) were white, 127 (13%) were black, and 54 (6%) were of other races (Table 1). Of the 5609 LPs, 1643 (29%) were traumatic, and 581 (10%) were bloody.

**Effects of Sex, Race, Age, Treatment Era, and Practitioner on the Odds of Traumatic and Bloody LP**

Sex had no effect on the proportion of traumatic or bloody LPs. Black race, age younger than 1 year, and early treatment era were associated with an increased risk of traumatic and bloody LP (Table 1 and Figure 1). Treatment protocol was significant in univariate analysis, but when treatment era was included in the multivariate analysis, the effect of treatment protocol disappeared (data available from authors on request). Also, there was no reduction in risk with recent use of glucocorticoid or l-asparaginase in either univariate or multivariate analysis (data available from authors on request); therefore, chemotherapy was not included in the final model. The 2 more experienced practitioner categories were associated with decreased odds of traumatic and bloody LP when compared with the 2 less experienced categories.

**Effect of Platelet Count at LP on the Odds of Traumatic and Bloody LP**

After adjusting for sex, race, age, treatment era, days since the previous LP, practitioner experience level, traumatic or bloody status of the previous LP, and platelet count at the previous LP, all platelet counts of 100×10^3/µL or less were associated with increased odds of traumatic and bloody LP (Table 2). When platelet counts were 100×10^3/µL or less, the odds of traumatic and bloody LP were not statistically significantly different among platelet categories. When we combine LPs performed at platelet counts less than 100×10^3/µL, the odds of traumatic and bloody LP are significantly increased compared with platelet counts of 100×10^3/µL or more.

**Table 1. Effects of Race, Sex, Age, Treatment Era, and Practitioner Experience on Traumatic and Bloody Lumbar Punctures (LPs) of Pediatric Patients With Acute Lymphoblastic Leukemia**

<table>
<thead>
<tr>
<th>Category</th>
<th>No. of Patients</th>
<th>No. of LPs</th>
<th>No. (%)</th>
<th>Odds Ratio (95% CI)†</th>
<th>No. (%)</th>
<th>Odds Ratio (95% CI)†</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Race</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>127</td>
<td>826</td>
<td>295 (36)</td>
<td>1.5 (1.2-1.8)</td>
<td>103 (12)</td>
<td>1.3 (1.0-1.7)</td>
</tr>
<tr>
<td>Other</td>
<td>54</td>
<td>340</td>
<td>100 (29)</td>
<td>1.1 (0.8-1.5)</td>
<td>40 (11)</td>
<td>1.2 (0.8-1.9)</td>
</tr>
<tr>
<td>White</td>
<td>775</td>
<td>4434</td>
<td>1248 (28)</td>
<td>1.0</td>
<td>438 (10)</td>
<td>1.0</td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>433</td>
<td>2493</td>
<td>773 (31)</td>
<td>1.1 (1.0-1.3)</td>
<td>281 (11)</td>
<td>1.1 (0.9-1.3)</td>
</tr>
<tr>
<td>Male</td>
<td>523</td>
<td>3116</td>
<td>870 (28)</td>
<td>1.0</td>
<td>300 (9.6)</td>
<td>1.0</td>
</tr>
<tr>
<td><strong>Age, y</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;1</td>
<td>34</td>
<td>236</td>
<td>113 (48)</td>
<td>2.3 (1.7-3.0)</td>
<td>55 (23)</td>
<td>2.6 (1.8-3.6)</td>
</tr>
<tr>
<td>≥1</td>
<td>922</td>
<td>5373</td>
<td>1530 (28)</td>
<td>1.0</td>
<td>526 (10)</td>
<td>1.0</td>
</tr>
<tr>
<td><strong>Era</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Early</td>
<td>731</td>
<td>4378</td>
<td>1362 (31)</td>
<td>1.4 (1.2-1.7)</td>
<td>493 (11)</td>
<td>1.6 (1.2-2.1)</td>
</tr>
<tr>
<td>Recent</td>
<td>225</td>
<td>1231</td>
<td>281 (23)</td>
<td>1.0</td>
<td>88 (7.1)</td>
<td>1.0</td>
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<tr>
<td><strong>Practitioner experience category</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 (Least)</td>
<td>790</td>
<td>304 (38)</td>
<td>1.4 (1.1-1.8)</td>
<td>120 (15)</td>
<td>1.3 (0.9-1.9)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>1619</td>
<td>544 (34)</td>
<td>1.3 (1.1-1.6)</td>
<td>201 (12)</td>
<td>1.3 (0.9-1.7)</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>1678</td>
<td>408 (24)</td>
<td>0.9 (0.7-1.0)</td>
<td>130 (7.8)</td>
<td>0.9 (0.7-1.2)</td>
<td></td>
</tr>
<tr>
<td>4 (Most)</td>
<td>1397</td>
<td>347 (25)</td>
<td>1.0</td>
<td>115 (8.2)</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td><strong>Total patients</strong></td>
<td>956</td>
<td>5609</td>
<td>1643 (29)</td>
<td>581 (10)</td>
<td>1.0</td>
<td></td>
</tr>
</tbody>
</table>

*CI indicates confidence interval; ellipses, data not applicable. Traumatic LP is defined as an LP in which samples of cerebrospinal fluid (CSF) contain at least 10 red blood cells (RBCs) per microliter. Bloody LP is defined as an LP in which samples of CSF contain at least 500 RBCs per microliter. Bloody LP was defined as an LP in which samples of CSF contain at least 500 RBCs per microliter. Unadjusted proportions are given.

†Estimated odds ratios and associated 95% CIs were adjusted for race, sex, age category, treatment era, platelet count at the current LP, days since the previous LP, status of the previous LP, platelet category at the previous LP, and practitioner experience category.

‡In 125 LPs, the practitioner who performed the procedure could not be determined; therefore, the results of the remaining 5484 LPs are reported.
100×10^3/µL, the OR for traumatic LP is 1.5 (95% CI, 1.2-1.8) when compared with LPs performed at platelet counts of 100×10^3/µL or more.

**Effect of Time Since the Previous LP**

Time since the previous LP had a significant effect on the incidence of traumatic and bloody LP (Figure 2). Fifty-five percent of the second LPs, which were typically performed within 1 to 4 days of the first, were traumatic and 26% were bloody, whereas only 19% of the first LPs were traumatic and 4.7% were bloody (Table 3). We evaluated the effect of the number of days since the previous LP on the risk of a subsequent traumatic or bloody LP. When an LP was performed 1 day after the previous LP, it was traumatic 75% of the time and bloody 33% of the time. The OR for traumatic LPs performed 1 day after the previous procedure compared with LPs more than 15 days apart was 10.8 and the OR for bloody LP was 7.2 (Table 3). Traumatic LP was more frequent if the procedure was performed within 15 days of a previous LP but returned to baseline thereafter (Figure 2), a trend consistent with the ORs estimated by logistic regression.

<table>
<thead>
<tr>
<th>Platelet Count, ×10^3/µL</th>
<th>No. of LPs</th>
<th>No. (%)</th>
<th>Odds Ratio (95% CI)†</th>
<th>No. (%)</th>
<th>Odds Ratio (95% CI)†</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-25</td>
<td>382</td>
<td>171 (45)</td>
<td>1.8 (1.3-2.4)</td>
<td>67 (18)</td>
<td>1.7 (1.1-2.5)</td>
</tr>
<tr>
<td>26-50</td>
<td>664</td>
<td>271 (41)</td>
<td>1.4 (1.1-1.8)</td>
<td>112 (17)</td>
<td>1.5 (1.0-2.0)</td>
</tr>
<tr>
<td>51-75</td>
<td>513</td>
<td>191 (37)</td>
<td>1.5 (1.1-1.9)</td>
<td>76 (15)</td>
<td>1.4 (1.0-2.1)</td>
</tr>
<tr>
<td>76-100</td>
<td>353</td>
<td>121 (34)</td>
<td>1.4 (1.1-1.9)</td>
<td>51 (14)</td>
<td>1.7 (1.1-2.5)</td>
</tr>
<tr>
<td>&gt;100</td>
<td>3594</td>
<td>855 (24)</td>
<td>1.0</td>
<td>266 (7.4)</td>
<td>1.0</td>
</tr>
</tbody>
</table>

All LPs with evaluable platelet counts‡ 5506 1609 (29) . . . 572 (10) . . .

*CI indicates confidence interval; ellipses, data not applicable. See asterisk footnote of Table 1.
†See dagger footnote of Table 1.
‡Of the 5609 LPs, 103 did not have an associated evaluable platelet count.

**Effects of the Traumatic or Bloody Status of the Previous LP and Platelet Count at the Previous LP**

A previous LP that was either traumatic or bloody increased the likelihood of subsequent LPs being traumatic or bloody (Table 4). After adjustment for all other risk factors by using logistic regression, the OR for traumatic LP was 1.6 (95% CI, 1.4-1.9) after a previous traumatic LP compared with a previous nontraumatic LP, and the OR for bloody LP was 1.9 (95% CI, 1.4-2.5) after a previous bloody LP. The platelet count at the previous LP was also an important risk factor. The OR for traumatic LP was 1.5 (95% CI, 1.1-2.0) and the OR for bloody LP was 1.6 (95% CI, 1.1-2.3) if the platelet count at the previous LP was 25×10^3/µL or less compared with those higher than 100×10^3/µL. The ORs were similarly high for subsequent traumatic and bloody LP if the platelet count at the previous LP was 26 to 50×10^3/µL compared with those higher than 100×10^3/µL. If the platelet count at the previous LP was higher than 50×10^3/µL, there was not a significantly increased risk. If more than 15 days had elapsed since the previous LP, the traumatic or bloody status and the platelet count at the previous LP had no effect on the outcome of the current LP (data available from authors on request).

**Combined Effects of Risk Factors on the Probability of Traumatic and Bloody LP**

Our data suggest that the lowest risk of traumatic or bloody LP occurs in a white patient whose LP is performed by an experienced practitioner more than 15 days after a previous LP at a platelet count of more than 100×10^3/µL. In the recent era with a nontraumatic previous LP performed at a platelet count of more than 100×10^3/µL, the multivariate model predicted that in this ideal setting, 9% of the LPs would be traumatic and 2% bloody. In this study, only 53 LPs were performed in this situation: 1 was traumatic and none were bloody. In contrast, the model pre-
predicts that a patient whose LP is performed in the most unfavorable conditions will have a 97% probability of traumatic and 84% probability of bloody LP. The single LP performed under these conditions was bloody.

**COMMENT**

This study evaluated an important problem with a common procedure and found modifiable risk factors for traumatic and bloody LP. In this large series, no neurologic complications of LP occurred, whether the procedure was bloody or not. However, traumatic and bloody LPs may indirectly lead to poor outcomes in pediatric patients with newly diagnosed ALL and circulating leukemic cells. Bloody LP may also be associated with iatrogenic meningitis when performed on patients with bacteremia. Moreover, bloody CSF obscures the diagnosis of central nervous system leukemia at the presentation of ALL. Therefore, attempts should be made to reduce the risk of traumatic and bloody LP.

The proportion of bloody LPs observed in this study (10%) is within the range reported in other pediatric studies (8%-19%); however, we made several novel observations in this study. The proportion of bloody LPs was greater among infants (23%) than among older pediatric patients (10%). The increased risk of bloody LP in infants may be due to technical difficulty in performing the LP that results from the smaller intervertebral space and the shallow depth of needle insertion required to reach the thecal sac. In a previous report that evaluated the first 2 LPs of 546 of the 956 patients included in this study, age younger than 1 year was associated with an increased risk of traumatic LP (OR, 1.7; 95% CI, 0.8-3.5). Because of the small number of evaluable procedures, the association did not achieve statistical significance.

The proportion of traumatic LPs was greater among black patients (36%) than white patients (28%), a difference that remained statistically significant even after controlling for all other risk factors (OR for traumatic LP, 1.5; 95% CI, 1.2-1.8). This difference may be the result of the greater lumbar lordosis in black patients compared with white patients, which makes optimal flexion of the spine for LP more difficult. Since most patients were either under conscious sedation or general anesthesia, any cultural differences in the response to medical interventions is not likely to play an important role in the observed effect of race on risk.

Procedures performed in the early treatment era were more likely to be traumatic or bloody (ORs, 1.4 and 1.6, respectively) than those performed during the recent era. The reduction in the proportion of traumatic and bloody LP occurred abruptly in May 1995, when several changes were implemented. Before that time, LPs were performed in the inpatient ward or outpatient clinic with no sedation or only conscious sedation; after that time, LPs were performed in a dedicated procedure area.

Figure 2. Relationship Between the Number of Days Since the Previous Lumbar Puncture (LP) and the Proportion of Traumatic and Bloody LPs

<table>
<thead>
<tr>
<th>Days Since the Previous LP</th>
<th>Traumatic LP</th>
<th>Bloody LP</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. (%)</td>
<td>Odds Ratio (95% CI)</td>
</tr>
<tr>
<td>1</td>
<td>246 (79)</td>
<td>10.8 (7.7-15.2)</td>
</tr>
<tr>
<td>2-3</td>
<td>218 (62)</td>
<td>5.8 (4.1-8.1)</td>
</tr>
<tr>
<td>4-7</td>
<td>1692 (56)</td>
<td>2.5 (2.1-3.0)</td>
</tr>
<tr>
<td>8-15</td>
<td>777 (25)</td>
<td>1.8 (1.5-2.3)</td>
</tr>
<tr>
<td>≥16</td>
<td>1720 (58)</td>
<td>1.0</td>
</tr>
<tr>
<td>First LP</td>
<td>9561 (49)</td>
<td>. . .</td>
</tr>
<tr>
<td>All LPs</td>
<td>5609</td>
<td>1643 (29)</td>
</tr>
</tbody>
</table>

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with designated staff for procedures and general anesthesia. These changes in anesthesia practice were made to decrease patient pain and anxiety; the beneficial effect on the risk of traumatic and bloody LP was discovered only as a result of this study. There were no systematic differences in the level of training of practitioners who performed LP during the 2 treatment eras, so we attribute the effect of treatment era to these changes. Practitioner experience level was a more important predictor of outcome than education level, which suggests that practice is important to achieve optimal skill in performing LP.

The platelet count is a strong predictor of traumatic and bloody LP; patients in all categories with platelet counts of $10^3/\mu L$ or higher is associated with a greater risk of traumatic and bloody LP. A short interval since the previous procedure is the strongest predictor of traumatic or bloody LP. The risk for both traumatic and bloody LP decreased as the interval between procedures increased. After 15 days, the unadjusted proportions of traumatic and bloody LPs were the same as those of the first LP (Figure 2). These findings suggest that blood leaks into the CSF after the procedure but clears during the subsequent 2 weeks. Furthermore, when the previous platelet count was $50 \times 10^3/\mu L$ or lower, the risk of traumatic or bloody LP was elevated, which implies that leakage of blood into the CSF of a thrombocytopenic patient is of greater magnitude or duration than that of a patient with a normal platelet count. If bacteremia occurs after LP, when blood is still leaking into the CSF, it may increase the risk of meningitis. In fact, Gaur et al found that of 12 patients with Bacillus cereus bacteremia, 4 developed concomitant meningitis. All 4 had undergone LP during the week before the bacteremia compared with none of the 8 patients whose bacteremia was not associated with meningitis. Hence, if medical circumstances allow, the subsequent procedure should be performed more than 15 days after the previous LP. In patients with definite evidence of leukemia (ie, the presence of circulating leukemic cells), we now administer intrathecal chemotherapy immediately after obtaining CSF for examination with the diagnostic LP, obviating the need for repeated LP for intrathecal chemotherapy in a short period. For other patients, we delay the LP and intrathecal chemotherapy until the diagnosis of leukemia is established.

Strengths of this study include a large number of patients and LPs, a variety of practitioners who performed the procedures, and a racially diverse group of pediatric patients. To our knowledge, this study is the first to assess the effects of thrombocytopenia, repeated procedures, and (indirectly) adequate anesthesia on traumatic and bloody LP, and our findings translate directly into recommendations for patient care. Our results remain essentially the same when the analysis is limited to patients with platelet counts of $25 \times 10^3/\mu L$ or higher and when bloody LP is defined by 200 or 1000 RBCs per microliter of CSF (data available on request from the authors).

In this study, most LPs were performed in children with ALL by using conscious sedation or general anesthesia; therefore, results should be applied with caution to other pediatric populations. However, LPs were performed by a variety of caregivers (pediatric oncologists, oncology fellows, oncology nurse

### Table 4. Effects of the Traumatic or Bloody Status of the Previous Lumbar Puncture (LP) and the Platelet Count at the Previous LP on Traumatic and Bloody LPs of Pediatric Patients With Acute Lymphoblastic Leukemia

<table>
<thead>
<tr>
<th>Previous platelet count, $10^3/\mu L$</th>
<th>No. of Evaluable LPs</th>
<th>Traumatic LP</th>
<th>Bloody LP</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. (%)</td>
<td>Odds Ratio (95% CI)†</td>
<td>No. (%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-25</td>
<td>371</td>
<td>163 (44) 1.5 (1.1-2.0)</td>
<td>68 (18)</td>
</tr>
<tr>
<td>26-50</td>
<td>638</td>
<td>262 (41) 1.3 (1.1-1.6)</td>
<td>117 (18)</td>
</tr>
<tr>
<td>51-75</td>
<td>494</td>
<td>190 (38) 1.2 (0.9-1.5)</td>
<td>74 (15)</td>
</tr>
<tr>
<td>76-100</td>
<td>329</td>
<td>113 (34) 1.1 (0.8-1.5)</td>
<td>47 (14)</td>
</tr>
<tr>
<td>&gt;100</td>
<td>2731</td>
<td>696 (25) 1.0</td>
<td>214 (8)</td>
</tr>
</tbody>
</table>

All LPs with evaluable previous platelet counts:

<table>
<thead>
<tr>
<th>No. (%)</th>
<th>Odds Ratio (95% CI)†</th>
</tr>
</thead>
<tbody>
<tr>
<td>520 (11)</td>
<td></td>
</tr>
</tbody>
</table>

*CI indicates confidence interval; ellipses, data not applicable. See asterisk footnote of Table 1.
†See dagger footnote of Table 1.
‡There were 4653 LPs with an evaluable outcome for the previous LP, but 90 of these did not have an evaluable previous platelet count.
practitioners, and residents); thus, results of procedures performed in other settings may be comparable. Another potential weakness of this study is the possible misclassification of the traumatic or bloody outcome of LPs. If an LP is difficult to perform and CSF is not obtained or is grossly bloody after several attempts, a more experienced practitioner may perform the procedure and obtain clear CSF. Alternatively, a traumatic or bloody LP by a more experienced practitioner may be the result of earlier failed attempts by a less experienced practitioner. A sensitivity analysis of such misclassification showed that if the outcomes of as many as 10% of LPs were misclassified, our results would change little. Another weakness is the lack of information about the LP needles used and the type of anesthesia administered and whether the procedure was difficult to perform or required multiple attempts.

In conclusion, unmodifiable risk factors for traumatic and bloody LP include black race, age younger than 1 year, a traumatic or bloody previous LP performed within 2 weeks, and a previous LP performed when the platelet count was 50 × 10^3/µL or less. Modifiable risk factors include procedural factors as reflected by the treatment era, platelet count, a short interval between LPs, and a less experienced practitioner.

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Analysis and interpretation of data: Howard, Gajjar, Cheng, Kritchevsky, Somes, Harrison, Ribeiro, Rivera, Sandlund, de Armenti, Razzouk, Pui.
Drafting of the manuscript: Howard, Gajjar, Cheng, Kritchevsky, Somes, Pui.
Critical revision of the manuscript for important intellectual content: Howard, Gajjar, Cheng, Kritchevsky, Somes, Harrison, Ribeiro, Rivera, Rubnitz, Sandlund, de Armenti, Razzouk, Pui.
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Obtained funding: Pui.
Administrative, technical, or material support: Razzouk, Pui.
Study supervision: Gajjar, Ribeiro, Sandlund, Razzouk, Pui.

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