Neuraxial Blockade and Hematoma in Cardiac Surgery*

Estimating the Risk of a Rare Adverse Event That Has Not (Yet) Occurred

Anthony M.-H. Ho, MD, MS; David C. Chung, MD; and Gavin M. Joynt, MBBCh

(CHEST 2000; 117:551–555)

Key words: cardiopulmonary bypass; regional techniques; risk; spinal hematoma

Abbreviations: CPB = cardiopulmonary bypass; MI = myocardial infarction

Although neuraxial anesthesia and analgesia techniques are widely used in many branches of surgery, critical care, and chronic pain, they have not enjoyed great popularity in operations involving cardiopulmonary bypass (CPB). This is mainly because of a concern for neuraxial hematoma and spinal cord injury when large doses of heparin are used. There are, however, many potential advantages of epidural and spinal anesthesia and analgesia in cardiac surgery. There is evidence to support improved hemodynamic stability,1–4 intense analgesia,4–8 early tracheal extubation,5,6,9 improved pulmonary function,5,6 enhanced coronary perfusion,9–12 decreased ischemia,9 improved ventricular function,13 and improved metabolic profile.1,3 Other advantages may include better pulmonary toilet, early ambulation, shorter ICU stay, and cost reduction. Sympathetic blockade may be particularly useful in minimally invasive cardiac surgery, although the possibility of unscheduled CPB remains a concern.

There are those who strongly oppose the use of neuraxial block in these patients because the effects of the combination of neuraxial blockade and high-dose heparin have not been adequately studied, and because the possible consequence of paraplegia from spinal hematoma is too severe to justify any potential gain. In contrast, it could be argued that the risk of clinically significant hematoma following CPB is very low when proper precautions are taken, and that cardiac surgery patients should not be denied the benefits of regional blockade. There is limited experience so far to support the latter claim.1–9,14,15

A large number of cardiac surgical procedures are performed every year. Attempts to quantify the potential gain and risks associated with neuraxial blockade therefore have important implications for patients, medical care providers, and planners. The objective of this paper is to use available literature to estimate the risk of clinically significant spinal hematoma after neuraxial blockade in conventional cardiac surgery.

Risk Estimation

There have been numerous reports on the use of spinal or epidural blocks in conventional cardiac surgery, but none have reported a case of clinically significant spinal hematoma.14–16 Neuraxial hematoma following instrumentation is, however, known to have occurred in other patients receiving anticoagulation therapy.17 We would therefore expect a similar or greater risk to occur in patients subjected to CPB during which profound anticoagulation is used. In other words, if enough cases of neuraxial blockade are performed, it should just be a matter of time before a case of clinically significant spinal hematoma occurs. What then is the predicted risk of clinically significant spinal hematoma? Based on available published data, we can estimate the "min-
imum” and the “maximum” risks for spinal and epidural blockade in cardiac surgery patients separately.

**Minimum Risk**

Estimating the minimum risk is relatively simple. It is reasonable to assume that the risks of neurologic complications from hematomas following epidural and spinal blockade in conventional cardiac surgery are no less than those reported for other surgical patients. The incidence of clinically significant spinal hematoma has been estimated with 95% confidence to be < 1 of 150,000 epidural anesthetics and < 1 of 220,000 spinal anesthetics for noncardiac surgical cases. These risks then are the expected minimum for neurologic injury associated with epidural and spinal blocks in conventional cardiac surgery.

**Maximum Risk**

To estimate the maximum risk, the probability technique described by Hanley and Lippmann-Hand for adverse events that have not yet occurred is employed.

If the risk of spinal cord injury from a neuraxial technique for cardiac surgery is \( r \), the probability of injury not occurring in a single case is \( 1 - r \). The probability \( (p) \) of this event not occurring in independent observations (statistical sample; \( n \)) is then \( (1 - r)^n \). If the technique has been performed in \( n \) cases of cardiac surgery without a single case of clinically significant spinal hematoma, how certain can we be that during the next \( n \) cases, there will not be at least one case of injury? To be 100% certain that the adverse event will not occur, \( p \), ie, \( (1 - r)^n \) is equal to 1. Under these conditions, \( r \) becomes zero (no risk). Obviously, we can never be 100% certain. Considering the seriousness of spinal hematoma, we would be wise to be conservative, and be only, say, 5%, or even only 1%, sure. We shall begin our analysis with 5%, a confidence limit generally accepted by medical convention. Thus, a finding that had at least a 5% chance of occurring is considered not that surprising, but anything with a smaller chance of occurring would be. The 95% confidence interval is a commonly used method of describing the likelihood of the finding. If we accept the above, then \( r \) at \( p = 0.05 \) would be the maximum risk, or the lower limit of the confidence interval. In other words, at \( p = 0.05 \), we are 5% confident of the fact that it was not chance that no hematoma had occurred after \( n \) cases. Stating it another way, we are 95% confident that the true risk of spinal hematoma is no more than the maximum risk at \( p = 0.05 \). We can therefore determine the maximum risk of an event, with a 5% error, that is compatible with \( n \) observations of nonoccurrence:

\[
(1 - r)^n = 0.05
\]

\[
1 - r = (0.05)^{1/n}
\]

\[
r = 1 - (0.05)^{1/n}
\]

Having arrived at the above equation, we can use the exponential function \( (e) \) and the natural logarithm \( (\ln) \) to solve it:

Let \( y \) be \( (0.05)^{1/n} \), and \( x \) be \( \ln(y) \), ie, \( x = \ln(0.05)^{1/12} \)

\[
= \frac{\ln(0.05)}{n}
\]

By definition:

\[
y = e^{\ln(y)}
\]

\[
\therefore r = 1 - y = 1 - e^{\ln(y)}
\]

Also by definition:

\[
e^x = \sum_{i=0}^{n} \frac{x^i}{i!} = x^0 + x^1 + \frac{x^2}{2} + \frac{x^3}{6} + \frac{x^4}{24} + \frac{x^5}{120} + \ldots
\]

\[
\therefore r = 1 - e^x = 1 - e^{\ln(y)}
\]

\[
= 1 - \left[ 1 + \frac{\ln (0.05)}{n} + \frac{[\ln(0.05)]^2}{2n^2} + \frac{[\ln(0.05)]^3}{6n^3} + \ldots \right]
\]

\[
= - \frac{\ln(0.05)}{n} - \frac{[\ln(0.05)]^2}{2n^2} - \frac{[\ln(0.05)]^3}{6n^3} - \ldots
\]

For large \( n \), such as \( > 30 \), the second and subsequent terms on the right side of the above equation are much less than the first,

\[
r \approx - \frac{\ln(0.05)}{n}
\]

\[
\approx \frac{2.9957}{n}
\]

\[
\approx \frac{3}{n}
\]

We can also use an alternative probabilistic approach. If \( r \) is the risk of spinal cord injury from a hemorrhagic complication, the expected number of coincidental occurrences among \( n \) cardiac cases is \( nr \). Assuming cardiac surgery and clinically significant spinal hematoma are independent, \( r \) is small, \( n \)
is large, and all events are reported, the probability distribution of the number of reported spinal injury (X) approximates a Poisson distribution with the parameter \( nr \). The probability \( (Pr) \) of observing \( y \) or more events is:

\[
Pr (X \geq y) = 1 - \sum_{k=0}^{y-1} e^{-nr} \frac{(nk)^k}{k!}
\]

For the probability of observing zero adverse event with 95% confidence:

\[
Pr (x = 0) = 1 - Pr (X \geq 1) = 0.05 = e^{-nr}
\]

\[
\therefore r = -\frac{\ln (0.05)}{n}
\]

Using both approaches, the risk \( (r) \) equals 3 divided by the number of observations \( (n) \).

Up to and including 1997,\(^{15}\) there had been almost 4,000 reported cases of epidural anesthesia or analgesia performed in cardiac surgical patients. An additional 558 cases were reported in 1998\(^{14}\) and 25 in 1999.\(^{9}\) There has not been a single reported case of clinically significant spinal hematoma.\(^{14-16}\) When the sum of these numbers, assuming they are accurate, is used to substitute for \( r \), the maximum risk of spinal cord injury from hematoma following epidural anesthesia and analgesia in conventional cardiac surgery approximates 3/4,583 or 1:1,528.

Subarachnoid anesthesia and analgesia has also been used in cardiac surgery.\(^{16,19-22}\) Again, no spinal hematoma has ever been reported.\(^{16,19-22}\) A similar analysis performed on approximately 10,840 cases\(^{16,19-21}\) would indicate that the maximum risk of hematoma causing neurologic injury following subarachnoid blocks in cardiac surgery approximates 3/10,840, or 1:3,610.

In summary, the risk of spinal injury from a neuraxial blockade-induced hematoma in conventional cardiac surgery has been estimated with 95% confidence to be from 1:150,000 to 1:1,500 for epidural blockade, and from 1:220,000 to 1:3,600 for spinal blockade.

Given the seriousness of spinal cord injury, some clinicians may demand a much more stringent confidence level, such as 99%. In other words, they are only 1% certain, as discussed earlier, that the absence of any spinal injury after \( n \) cases is not due to chance. The 99% confidence level can be calculated by replacing 0.05 in all of the above equations with 0.01 to arrive at \( r = 4.6/n.\)\(^{18}\) The resulting maximum risks associated with epidural and spinal blockade are considerably higher, 1:1,000 and 1:2,400, respectively.

**Discussion**

It must be remembered that all of the risks calculated above only indicate what might reasonably be expected, based on available data. The analysis does not take into account the probability that the total number of neuraxial blocks for cardiac surgery that has been performed worldwide is higher, and the possibility that cases of spinal/epidural hematoma have not been reported. In fact, even the now well-accepted estimates of the incidences of hematoma after spinal and epidural blocks in noncardiac cases are also subject to these flaws. All of the risks calculated above are therefore only approximate at best, and this discussion should serve primarily as a reminder against premature declarations of the safety or danger of neuraxial techniques. Increased accuracy of risk prediction can only be achieved by more and accurate data acquisition. Reporting and publication of data relating to neuraxial blockade and the establishing of a national or international complication registry is to be encouraged. A global confidential survey of all centers that practice neuraxial techniques during cardiac surgery may yield additional information to allow a more accurate estimate of risk.

To achieve zero occurrence of spinal injury thus far, clinicians have taken numerous precautions:\(^{1-5,7,14-17,21,23-25}\) (1) normalization of coagulation before instrumentation; (2) avoidance of repeated attempts; (3) postponement of surgery for 24 h after bloody tap; (4) instrumentation \( \geq 1 \) h before systemic heparinization (most authors insert the epidural catheter the day before surgery); (5) optimization of hemostasis after CPB; (6) removal of epidural catheter only after normal hemostasis has been restored postoperatively; (7) close neurologic surveillance; (8) use of a midline technique; (9) administration of saline solution through the needle to distend the epidural space before insertion of the catheter; and (10) neuraxial instrumentation postoperatively only after normalization of coagulation. Significant breaching of such protocols will likely increase the risk.

The above estimates are conservative, based on accepted limits of chance, and the true risks could be considerably lower. For some clinicians, however, one single case of spinal hematoma is too many, and the risks calculated above are simply not low enough.
especially when the benefits of neuraxial blockade in cardiac surgery have not yet been adequately substantiated. For understandable reasons, we may be less intolerant of myocardial infarction (MI), respiratory failure, or even death after cardiac surgery, than of paraplegia after an otherwise successful cardiac repair. Fear of spinal hematoma will thus continue to discourage the use of regional techniques, and thus hamper the accumulation of experience and data.

The acceptance of any technique into routine practice depends ultimately on evidence that its associated risks can be justified by improved outcome measures. Having gained some appreciation of the most feared risk of neuraxial blockade, we could examine its potential benefits. There is data to suggest that ischemia or infarction may be reduced by the use of neuraxial blockade during cardiac surgery. Previous studies in medical and noncardiac surgical populations have demonstrated that sympathetic blockade, either through regional blockade or systemic medications, results in reduced myocardial ischemia, infarction, and morbidity.10–13,15,26,27 Moreover, serum troponin levels are decreased when thoracic epidural analgesia is used in coronary artery bypass surgery,4 and elevated serum troponin levels are sensitive and specific for MI after cardiac surgery.28 Unfortunately, large enough trials that are able to demonstrate reduced MI and mortality from the use of neuraxial blocks in cardiac surgery are lacking. (A conservative estimate of the incidence of MI would be approximately 4%,29 A power analysis could be performed for a type I error (α, one-tailed) of 0.05 and a power of 0.80 (β = 0.20). It would require 398, 997, or 4,373 patients in the control and in the study groups to show that neuraxial blockade reduces the incidence of MI to 1%, 2%, or 3%, respectively.)

Let us assume that the incidence of MI after coronary artery bypass surgery is 4%.29 If the mortality rate of postoperative MI associated with conventional coronary bypass surgery is estimated to be 13%,30 and neuraxial blockade results in an absolute reduction of 0.5% in the incidence of MI, then one death would be avoided for every 1,540 patients (because $1,540 \times (4\% - 3.5\%) \times 13\% = 1$). By comparison, we are 95% and 99% confident that there will be no more than one case of hematoma (and potential paraplegia) for every 1,500 and 1,000 cases, respectively, of bypass surgery. Based on these estimates, neuraxial blockade is quite possibly a useful adjunct in conventional cardiac surgery.

In conclusion, it is possible to estimate the risk of a rare adverse event that has not (yet) occurred. In the case of neuraxial hematoma due to regional blockade for conventional cardiac surgery, there may be a sufficiently acceptable risk/benefit ratio to justify a large-scale study on selected patients.

ACKNOWLEDGMENT: Thanks are extended to Ms. L. M. Yu, MS, of the Centre for Clinical Trials and Epidemiological Research of the Chinese University of Hong Kong for her helpful comments.

References


21 Hall RI, Adderley NL. Intrathecal morphine for analgesia following coronary artery bypass surgery (CABG) [abstract]. Can J Anaesth 1999; 46:A3B.


