Evaluation of Pulse Cooximetry in Patients Undergoing Abdominal or Pelvic Surgery


ABSTRACT

Background: Intraoperative transfusion decisions generally are guided by blood loss estimation and periodic invasive hemoglobin measurement. Continuous hemoglobin measurement by pulse cooximetry (pulse hemoglobin; Rainbow® SET Pulse CO-Oximeter, Masimo Corporation, Irvine, CA) has good agreement with laboratory hemoglobin in healthy volunteers and could aid transfusion decision-making. Because intraoperative physiology may alter performance of this device, this study investigated pulse hemoglobin during surgery.

Methods: Ninety-one adult patients undergoing abdominal or pelvic surgery in which large blood loss was likely were studied. Time-matched pulse hemoglobin measurements were recorded for each intraoperative arterial hemoglobin measurement obtained. Agreement between measurements was assessed by average difference (mean ± SD, g/dl), linear regression, and multiple measures Bland-Altman analysis.

Results: The average difference between 360 time-matched measurements (bias) was 0.50 ± 1.44 g/dl, with wider limits of agreement (−2.3 to 3.3 g/dl) than reported in healthy volunteers. The average difference between 269 paired sequential pulse and arterial hemoglobin changes was 0.10 ± 1.11 g/dl, with half between −0.6 and 0.7 g/dl of each other. The bias was larger in patients with blood loss of more than 1,000 ml; hemoglobin less than 9.0 g/dl; any intraoperative transfusion; or intraoperative decrease in arterial hemoglobin at the time of sampling ≥2 g/dl (all P < 0.001). The range of bias was narrower at deeper anesthesia (P < 0.001).

Conclusions: Evaluation of the sensor and software version tested suggests that although pulse cooximetry may perform well in ambulatory subjects, in patients undergoing surgery in which large blood loss is likely, an invasive measurement should be used in transfusion decision-making.

Patients undergoing major abdominal or pelvic surgery can experience significant intraoperative blood loss. There is growing evidence that perioperative transfusion is associated with postoperative morbidity in at least some surgical patients.1,2 However, perioperative anemia is associated with increased risk for morbidity,3,4 particularly in patients with comorbid conditions.5,6 The results of studies investigating the outcome impact of perioperative transfusion vary.7–11 The appropriate target range for hemoglobin during surgery is likely patient-specific,12–15 but most patients will tolerate hemoglobin in the range of 7–9 g/dl with little evidence to support transfusion to hemoglobin greater than 10 g/dl.16,17 Maintaining hemoglobin within a target range during surgery by titrated transfusion could limit the

What We Already Know about This Topic

• Continuous on-site measurement of hemoglobin by pulse cooximetry has been shown to agree fairly well with laboratory hemoglobin measurements in volunteers.

What This Article Tells Us That Is New

• This study in 91 surgical patients demonstrated a weak correlation between paired changes in arterial hemoglobin as measured by arterial blood gas cooximetry and noninvasive continuous pulse cooximetry. Differences between both measurement modalities were most pronounced in patients with larger blood loss or lower arterial hemoglobin values.
potentially adverse effects of anemia and transfusion and thus be associated with decreased complications.

Continuous intraoperative hemoglobin measurement could provide monitoring guidance during surgery to aid in maintaining hemoglobin within a target range. The nadir sometimes encountered with rapid blood loss and intermittent hemoglobin measurements may be prevented, whereas excessive blood product administration could be avoided if transfusion were held once the target hemoglobin was obtained. Currently, transfusion decisions are guided by visual estimation of surgical blood loss with periodic hemoglobin measurement using invasive means, such as point-of-care testing, clinical laboratory testing, or arterial blood gas determination of hemoglobin (arterial hemoglobin). A Food and Drug Administration-approved device (Rainbow® SET Pulse CO-Oximeter; Masimo Corporation, Irvine, CA) provides continuous pulse hemoglobin (SpHb) measurement derived from pulse cooximetry. SpHb measured by the device has a published average root mean square difference of 0.94 g/dl compared with reference laboratory methods in adult volunteers undergoing hemodilution. In that study, the average study-induced decrease in hemoglobin was 2.4 ± 0.8 g/dl. That study design induced a degree of hypervolemic hemodilution to cause an approximately 30% decrease in hemoglobin by withdrawal of ± 500 ml blood followed by rapid administration of as much as 30 ml/kg crystalloid. The hemoglobin decrease during surgery is initiated by blood loss and may be associated with different cardiovascular physiology than that of hypervolemic hemodilution. We hypothesized that the physiologic changes induced by anesthesia, surgery, surgical blood loss, and intraoperative fluid administration may alter performance of this device in ways not seen in healthy volunteers, which could lead to larger differences between SpHb and arterial hemoglobin. In addition, we hypothesized that these differences may vary with identifiable individual or intraoperative characteristics. This study was designed to investigate the performance of SpHb in patients undergoing abdominal or pelvic surgery in whom large blood loss was likely.

Materials and Methods

The Institutional Review Board of Loma Linda University (Loma Linda, CA) approved this departmentally sponsored, convenience sample, prospective study. A departmental quality review of transfusion practices was done to identify combinations of scheduled procedure and surgical team that were more likely to be associated with large enough blood loss to decrease a patient’s hemoglobin into the range in which transfusion may be considered (8–10 g/dl). Some of these combinations included extensive resection of abdominal or pelvic cancers or open abdominal major vascular procedures by specialists in high-risk patient care. In these combinations, more than 60% of patients were transfused an average of 3.5 units, and nearly 25% had a documented hemoglobin decrease consistent with blood loss of more than 20% of estimated blood volume. We chose to study SpHb to arterial hemoglobin differences in surgical patients scheduled for one of these combinations to obtain a study group with blood loss large enough to put the patient at risk for transfusion. Consenting adult patients scheduled for an identified combination at Loma Linda University Medical Center were studied. Exclusion criteria were coagulopathy, hemoglobinopathy, and cardiac dysrhythmias.

Patients underwent general endotracheal anesthesia with agents chosen by the anesthesia team. Routine monitors, per American Society of Anesthesiologists Guidelines, were used during the perioperative period. When the patient was monitored by processed electroencephalography (Sedline, Masimo Corporation), moderate anesthesia (Patient State Index, 30–50) was targeted. A Masimo Radical-7 Pulse CO-Oximetry sensor (revision E) was placed on the third finger on the same side as the arterial catheter as per manufacturer recommendations. The sensor was shielded from outside light with a manufacturer-specified optical shield. SpHb and perfusion index were monitored continuously throughout each procedure. A radial arterial catheter was placed for blood pressure monitoring and arterial hemoglobin analysis using a cooximeter (Radiometer ABL800; Radiometer, Copenhagen, Denmark), at approximately 60-min intervals, as is our practice for the types of procedures included in this study. Time-matched SpHb was recorded when arterial hemoglobin samples were obtained during the procedure. Intraoperative fluid administration was guided by assessing stroke volume variation provided by a computerized arterial pulse waveform cardiac output device (FloTrac; Edwards Lifesciences, Irvine, CA) as a sign of fluid responsiveness during abdominal or pelvic surgery using positive pressure ventilation, in addition to usual clinical indicators of intravascular volume status. Stroke volume variation ≥12% for at least 2 consecutive min was considered an indication for fluid administration by protocol with either colloid or crystalloid to minimize hypovolemia. Transfusion of blood products was at the discretion of the attending anesthesiologist caring for the patient, with intraoperative transfusion given if needed to maintain hemoglobin between 8 and 10 g/dl during surgery. Estimated blood volume was calculated using the method of Lemmens et al.,23 which adjusts blood volume based on body mass index. Estimated blood loss as a proportion of estimated blood volume (EBL%) was calculated based on the estimated blood loss recorded (as determined by the anesthesia providers) divided by the estimated blood volume. Hemoglobin decrease was determined as the difference between preoperative and the last arterial hemoglobin measurements. Transfusion of packed erythrocytes was recorded as the volume administered. Percent change in erythrocyte volume was calculated based on erythrocyte volume using preoperative hemoglobin, hemoglobin decrease, and erythrocyte transfusion volume corrected for the hematocrit of packed erythrocytes.
**Statistical Analysis**

The primary measurement was the difference between SpHb and arterial hemoglobin (bias) at each paired measurement expressed as mean ± SD g/dl. This calculation will yield a positive number when SpHb is higher than arterial hemoglobin and a negative number when SpHb is less than arterial hemoglobin. We were interested in investigating SpHb to arterial hemoglobin differences in patients with differing intraoperative blood loss, including some with large blood loss. It was determined that a sample size of 20 in the group with blood loss more than 20% would show that an SpHb to arterial hemoglobin difference of 0.6 g/dl compared with patients with low intraoperative blood loss was significant with power set at 0.8 and \( P = 0.05 \). Based on our departmental quality review of transfusion practices, we calculated 90 patients would need to complete the study to get 20 in whom intraoperative blood loss was more than 20%.

Statistical analysis was performed using computerized software (JMP for Macintosh 8.0.2; SAS Institute Inc, Cary, NC; GraphPad Prism for Macintosh 5.0d; GraphPad Software, La Jolla, CA; MedCalc 11.6.1; MedCalc Software, Mariakerke, Belgium). Multiple measures Bland-Altman analysis of agreement between SpHb and arterial hemoglobin was performed and reported as bias between measurements and the average of the measurements with ±1.96 SD limits of agreement. Because arterial hemoglobin often is used in clinical practice to provide hemoglobin measurement as a guide to transfusion during surgery in which large blood loss is likely and because hemoglobin determination by the Radiometer ABL800 is highly accurate, differences between SpHb and arterial hemoglobin were compared with arterial hemoglobin by linear regression. Possible correlations between individual and intraoperative characteristics, based on cutoff limits identified in the literature for specific characteristics, were evaluated by linear regression analysis. Additional comparison of the mean SpHb to arterial hemoglobin differences found in these subgroups was done using ANOVA or Student \( t \) test (continuous normally distributed data), or chi-square analysis (ordinal and nominal bivariate data). A \( P \) value \( \leq 0.05 \) was considered significant.

**Results**

Ninety-two patients enrolled in this study, with equipment malfunction preventing SpHb monitoring in one patient. Characteristics of the 91 patients included for analysis are shown in table 1. The recorded blood loss estimate was less than 500 ml in 39 patients, between 500 and 1,000 ml in 32 patients, and more than 1,000 ml in 17 patients. The average EBL% was 16 ± 22% (median 11%, range 0–179%) and was more than 20% of estimated blood volume in 21 (23%) patients. The calculated percent erythrocyte volume change was somewhat larger at 19.4 ± 10.7% (median 19.5%, range −5% to 42%), and more than 25% in 28 (31%) patients. EBL% did not correlate with the number of paired samples (\( R^2 = 0.14 \)), or surgery length (\( R^2 \) less than 0.01). When evaluated as groups, patients who had six paired samples had larger EBL% than did those with two, three, or four paired samples (\( P < 0.01 \)) but not those with other numbers of paired samples. Thirty-five patients received at least 1 unit of packed erythrocyte transfusion during surgery, with an average hemoglobin decrease of 2.1 ± 1.6 g/dl despite transfusion. Of the 56 patients who were not transfused, the average hemoglobin decrease was 2.9 ± 1.4 g/dl (median 2.7; range 0–6.7 g/dl), and 21 of these patients had at least one arterial hemoglobin value ≤10 g/dl.

A total of 360 time-matched SpHb and arterial hemoglobin measurements were analyzed. The range of arterial hemoglobin was 6.0–16.0 g/dl (median 10.3 g/dl). Arterial hemoglobin was more than 10 g/dl in 210 measurement pairs, between 8 and 10 g/dl in 123 measurement pairs, and less than 8 g/dl in 27 measurement pairs. The median number of arterial samples per patient was four, with a range of one (in three patients) to nine (in one patient). The median interval between baseline and the next sample was 48 min, whereas the interval between subsequent samples was approximately 60 min to the seventh hour of surgery. The mean difference between measurements was 0.50 ± 1.44 g/dl. Multiple measures Bland-Altman analysis of agreement between SpHb and arterial hemoglobin is shown in figure 1. The bias was 0.50 g/dl with ±1.96 SD limits of agreement −2.3 to 3.3 g/dl. The distribution of SpHb and arterial hemoglobin measurements and the SpHb to arterial hemoglobin difference compared with arterial hemoglobin are shown in figure 2. Linear regression analysis of SpHb to arterial hemoglobin difference resulted in \( R^2 = 0.48 \) with root mean square error of 1.30 g/dl. SpHb was within 1 g/dl of the arterial hemoglobin value in 51.4%, within 1.5 g/dl in
68.3%, and within 2 g/dl in 83.3% of the paired measurements. The SpHb to arterial hemoglobin bias was higher at lower arterial hemoglobin values (fig. 2B). Bias was also higher in 72 measurement pairs obtained when arterial hemoglobin at the time of sampling was more than 1 g/dl less than the first intraoperative arterial hemoglobin (1.10 ± 1.53 g/dl) compared with smaller decreases or increases (0.47 ± 1.37 g/dl, P = 0.002).

In 88 patients with more than one paired measurement, sequential changes in both arterial hemoglobin and SpHb were calculated and compared. Figure 3 shows the distribution of the 269 sequential paired measurements (R² = 0.31). The average difference between paired sequential changes in SpHb and arterial hemoglobin was 0.10 ± 1.11 g/dl, with differences between SpHb change and arterial hemoglobin change ranging from −3.7 to 5.5 g/dl. In 136 (52%) of the sequential measurements, the difference between the change in arterial hemoglobin and the paired change in SpHb was between −0.61 and 0.61 g/dl. In 192 sequential pairs, the changes in arterial hemoglobin and SpHb were in the same direction: no change, decrease, or increase in both measures. In 42 of the paired sequential changes, SpHb increased when arterial hemoglobin decreased, including 14 (5.2%) in which SpHb increased when arterial hemoglobin decreased by more than 1 g/dl. These discordant changes occurred at arterial hemoglobin values ranging from 7.7 to 14.7 g/dl (median 9.6 g/dl).

Time of monitoring did not alter the SpHb to arterial hemoglobin bias (fig. 4A). The mean bias was the same at all sample intervals (baseline = 0.54 ± 1.45 g/dl; first hour = 0.96 ± 0.92 g/dl; second hour = 0.42 ± 1.44 g/dl; third hour = 0.12 ± 1.49 g/dl; fourth hour = 0.61 ± 1.27; fifth hour = 0.35 ± 1.56 g/dl; sixth hour = 0.11 ± 1.46 g/dl; seventh hour or longer = 0.76 ± 0.41 g/dl; P = 0.26 ANOVA). Although the number of paired measurements did not correlate with bias (R² = 0.04), bias was larger at the sixth paired measurement than with the first or second, but not other, measurement pairs (P = 0.003). When evaluated as groups, patients who had six paired measurements had higher mean bias than those with two, three, or four paired measurements (P < 0.01) but not those with other numbers of paired measurements (fig. 4B). For each patient, the mean and range of SpHb to arterial hemoglobin bias was calculated (fig. 4C). In 19 of 88 patients with two or more measurement pairs, the SpHb to arterial hemoglobin bias was within ±1 g/dl for all measurement pairs. The remaining patients had bias outside this range, including 32 patients with at least one paired measurement with positive bias and one paired measurement with negative bias or a range between minimum and maximum bias of more than 2 g/dl. These 32 patients did not differ in age, gender, body mass index, surgical procedure, or surgery length (347 ± 155 min vs. 265 ± 140 min, P = 0.06) but had greater blood loss (1,169 ± 1,358 ml vs. 373 ± 237 ml, P = 0.002), larger EBL% (26.0 ± 0.3% vs. 7.3 ± 0.1%, P = 0.003), greater documented decrease in arterial hemoglobin (2.6 ± 1.7 g/dl vs. 1.1 ± 0.9 g/dl, P < 0.001), more transfusion of erythrocytes (638 ± 1,057 ml ±
Fig. 3. Linear regression analysis of 269 paired changes in sequential measures of pulse hemoglobin (SpHb) and arterial hemoglobin in 91 patients undergoing abdominal or pelvic surgery ($R^2 = 0.31$; root mean square error 0.92 g/dl; slope = 0.49, 95% confidence interval 0.41–0.58 shown by dashed lines). In 179 of the 269 pairs, the sequential changes in arterial hemoglobin and SpHb were in the same direction: no change, decrease, or increase in both measures. In 136 of the paired sequential changes, the difference between the change in SpHb and the change in arterial hemoglobin was between −0.61 and 0.61 g/dl. In 41 paired measurements (shaded area), SpHb increased when arterial hemoglobin decreased, including 14 in which SpHb increased when arterial hemoglobin decreased by more than 1 g/dl.

920 vs. 147 ± 293 ml, $P = 0.02$), and a larger number of samples (4.8 ± 1.7 pairs vs. 3.2 ± 1.3 pairs, $P < 0.001$) compared with the 19 patients in whom bias was within ±1 g/dl for all paired measurements.

Mean bias and linear correlation analysis was performed based on subgroups defined for individual and intraoperative characteristics (see table, Supplemental Digital Content 1, http://links.lww.com/ALN/A794, which is a table of results for characteristics evaluated in this study). Several characteristics were found to have a relationship to bias. As shown in figure 5A, the mean SpHb to arterial hemoglobin bias was less at deeper levels of anesthesia (Patient State Index less than 30; −0.05 ± 1.2 g/dl) compared with moderate (Patient State Index 30–50, 0.59 ± 1.41 g/dl) or light (Patient State Index 50–60, 1.48 ± 1.48 g/dl) anesthesia levels ($P < 0.001$) and was within 1.5 g/dl in 82% of 71 pairs when Patient State Index was less than 30. The mean SpHb to arterial hemoglobin bias was larger when mean arterial blood pressure was less than 70 mmHg compared with greater than 90 mmHg (0.86 ± 1.5 g/dl vs. 0.01 ± 1.5 g/dl, $P = 0.002$). As shown in figure 5B, the SpHb to arterial hemoglobin bias was higher when arterial hemoglobin was less than 9 g/dl (1.31 ± 1.25 g/dl) compared with 9–12 g/dl (0.49 ± 1.36 g/dl) or more than 12 g/dl ($0.43 ± 1.31; P < 0.001$). The positive difference in SpHb was larger at lower arterial hemoglobin: in the 27 paired measurements in which arterial hemoglobin was less than 8.0 the average difference was 1.5 ± 0.9 g/dl. The average SpHb to arterial hemoglobin bias was larger in patients whose estimated blood loss was more than 1,000 ml (fig. 5C). Bias was lower in paired measurements obtained when the perfusion index was ≤1 (n = 49; −0.14 ± 1.67 g/dl) compared with between 1 and 4 (n = 185; 0.66 ± 1.45 g/dl) or more than 4 (n = 126; 0.52 ± 1.27 g/dl, $P = 0.002$). Bias was not related to either stroke volume variation or pleth variability index.

**Discussion**

Continuous noninvasive hemoglobin trend monitoring could provide valuable guidance regarding blood loss and the need for transfusion therapy during surgery. The need for invasive hemoglobin measurements could be reduced if SpHb is consistent with other measures such as arterial hemoglobin. It may also prove beneficial by allowing tighter
control of intraoperative fluid administration and blood product therapy, thereby maintaining patients within a target hemoglobin range. However, to supplant current hemoglobin monitoring practices, SpHb should accurately represent both true hemoglobin at any given point in time and the trend of hemoglobin throughout surgery. The published precision of SpHb, \( \pm 0.94 \text{ g/dl} \) of the laboratory derived hemoglobin value,\(^1\) may be a reasonable degree of accuracy to provide guidance for therapeutic transfusion decisions, particularly for values within the intraoperative target hemoglobin range used here (8–10 g/dl).

Information from SpHb might provide insight about the rate of bleeding and resuscitation if the trend of SpHb to arterial hemoglobin remains consistent during surgery. Clearly, clinicians could use consistent bias to approximate the arterial hemoglobin value from the SpHb value. However, we found weak correlation between paired changes in arterial hemoglobin and SpHb overall. In addition, we found larger differences between SpHb and arterial hemoglobin in patients with larger blood loss or lower arterial hemoglobin values. Our analysis showed higher SpHb than arterial hemoglobin at lower hemoglobin values. When arterial hemoglobi-
globin was less than 9.0 g/dl, the average positive difference in SpHb was 1.3 g/dl, and this positive difference was larger when arterial hemoglobin was less than 8.0 (1.5 g/dl). This positive difference indicates SpHb values greater than arterial hemoglobin values at these low levels, and is potentially large enough to affect transfusion decisions. Of note, the difference between SpHb and arterial hemoglobin in sequential pairs obtained from some individuals varied considerably and was not consistently negative or positive in sequential paired measurements during the course of a surgical procedure (fig. 4C). We did not find a systematic relationship between bias and the number of paired measurements. When considered as a group, patients who had six paired measurements had higher mean bias than did those with two to four but not those with more than six measurement pairs. It is likely that blood loss explains this finding, because bias was higher at lower arterial hemoglobin values, which were found more often in patients with higher EBL%. Patients with six measurement pairs had higher EBL% and lower average arterial hemoglobin at the time paired measurements were done than all others. A wider range of bias correlated only to intraoperative characteristics such as surgery duration and estimated blood loss. In addition, in only 19 patients was mean, minimum, and maximum bias within ±1 g/dl in all paired samples. We were unable to identify any individual characteristics that would allow the clinician to predict in which patients the SpHb would be accurate. The lack of a consistent relationship between individual bias and individual characteristics limits the ability to predict when the SpHb to arterial hemoglobin difference will be larger or when the difference between measures in a given patient will change in either a positive or negative direction in sequential samples. This limits the utility of SpHb as a hemoglobin trend monitor during abdominal or pelvic surgery in which large amounts of blood loss or low intraoperative hemoglobin values are likely.

The subjects in this study underwent procedures in which bleeding was likely, and most were either transfused or had an intraoperative decrease in arterial hemoglobin to a level at which intraoperative transfusion may have been considered. In these patients, 83% of SpHb measurements were within ±2 g/dl of the arterial hemoglobin value, which is different from the reported 90% within 1.5 g/dl in a study conducted in healthy volunteers. The range of ±1 g/dl was found in 51.4% of measurements. Our limits of agreement are similar to those found in 20 patients undergoing spine surgery, but the specific intraoperative conditions, amount of blood loss, and duration of surgery in our patients may be different from those in patients undergoing other types of surgical procedures, which may limit the ability to compare results between studies. However, in samples from 62 intensive care patients (47% surgical), SpHb was found to have better agreement with arterial hemoglobin than we found. In the intensive care patients, SpHb was within ±1 g/dl of arterial hemoglobin in 85% of paired samples, and bias from Bland-Altman analysis was 0.0 g/dl with limits of agreement of ±1.0 g/dl. We found a greater difference between SpHb and arterial hemoglobin in patients who had more estimated blood loss, larger intraoperative arterial hemoglobin decreases, or received erythrocyte transfusion, and when mean arterial pressure was lower. In addition the SpHb to arterial hemoglobin limits of agreement were narrower at deeper levels of anesthesia. In a reported subgroup analysis of intensive care patients, bias and limits of agreement were larger in patients receiving norepinephrine at the time of sampling. When taken together, these results suggest that surgical conditions, blood loss, transfusion, or deep anesthesia change peripheral circulatory physiology compared with those of the ambulatory state. These changes could explain in part why our findings differ from those reported in healthy volunteers and may warrant additional study.

Interpretation of our results may be limited by the use of arterial blood gas cooximeter hemoglobin, instead of a reference laboratory standard to compare to SpHb. This reflects intraoperative care for many patients undergoing surgical procedures in which large blood loss is likely. In addition, the device used in this study for arterial blood gas analysis has a published precision of 0.06 g/dl at hemoglobin of 11.3 g/dl. The device used for this study undergoes quality checks every 8 h, with documented accuracy of ±0 at 8.3 g/dl; ±0.1 at 13.1 g/dl, and ±0.2 at 19.7 g/dl within a period of subject enrollment. Our sample size may have prevented detection of subtle correlations between intraoperative or patient characteristics and either the magnitude of difference between SpHb and arterial hemoglobin or changes in bias between sequential paired measurements.

Hemoglobin measurement based on pulse cooximetry appears to perform reasonably well in ambulatory subjects, intensive care patients, and some of our surgical patients. However, evaluation of the sensor and software version tested here suggests that in patients undergoing surgery in which large blood loss is likely, an invasive measurement method, such as intraoperative arterial hemoglobin rather than SpHb, should be used as part of transfusion decision-making. Additional study is warranted to determine what factors may lead to larger SpHb to arterial hemoglobin differences, particularly in patients with large blood loss and fluid resuscitation. This should allow for improvement in pulse cooximetry algorithms as this technology continues to evolve. It seems prudent to recommend that future software and sensor revisions undergo study designed to clarify the performance of this technology in patients undergoing surgery in which large blood loss is likely.

References


2. Spahn DR. Anemia and patient blood management in hip and knee

Anesthesiology 2012; 116:65–72

Applegate II et al.


