

## Gender Affects Report of Pain and Function after Arthroscopic Anterior Cruciate Ligament Reconstruction

Andreas H. Taenzer, M.D.,\* Cantwell Clark, M.D.,† Craig S. Curry, M.D.\*

**Background:** Gender-related differences in pain have been clearly shown in experimental settings. Clinical studies of such differences have produced conflicting findings. No studies have shown a significant difference in pain experience associated with differences in functional outcomes. Arthroscopic anterior cruciate ligament reconstruction (AACL R) produces pain of moderate intensity and provides a useful setting for examining gender-related differences in pain and function.

**Methods:** This study was a retrospective review of prospectively gathered data collected for a continuous quality improvement program and involved all patients who underwent AACL R at a single outpatient facility since June 1992. Anesthetic, surgical, and perioperative management techniques were standardized. Using a questionnaire, all patients were routinely asked to record pain scores, narcotic consumption, and whether they were able to perform a standardized straight leg-raising maneuver on each of the first 5 postoperative days.

**Results:** A total of 736 patients were enrolled for surgery, 58% of whom completed the entire 5-day questionnaire. Women reported higher pain scores at rest as well as with activity on postoperative day 1 compared with men ( $P < 0.005$ ). In addition, fewer women were able to perform the straight leg-raising maneuver on postoperative day 1 ( $P = 0.002$ ) and postoperative

day 2 ( $P = 0.004$ ). There was no difference in the amount of narcotics consumed at any time during the study period.

**Conclusions:** Women seem to experience greater intensity of pain after AACL R that is associated with a decrease in an intermediate measure of functional outcome. These differences may result from differences in either response to analgesics or neuroprocessing. (Key words: Knee; repair; recovery.)

SEVERAL studies have described gender-related differences in pain report to experimental noxious stimuli, with most reporting lower pain thresholds or higher pain ratings for women.<sup>1-4</sup> Studies of gender-related differences in pain reports in clinical settings have produced contradictory results.<sup>5</sup> None of these studies has examined the association of reports of pain and ability to function.

We have been gathering data for continuous quality improvement on all patients undergoing arthroscopic anterior cruciate ligament reconstruction (AACL R) using standardized surgical, anesthetic, and pain management protocols since June 1992. We have found this to be a useful model to study pain and have previously reported pain scores and their impact on function after this surgery.<sup>6</sup> As these patients report a significant amount of pain that is clearly associated with impaired function, patients undergoing this type of operation provide a useful model of the interaction between pain and function. The current study was designed to examine the effect of gender on pain and function after AACL R.

## Materials and Methods

### Patient Selection

After receiving approval from the Institutional Review Board for Human Studies at the Maine Medical Center, data collected from an ongoing continuous quality-improvement project were reviewed. Since June 1992, all patients ( $N = 736$ ) who had undergone AACL R were asked to participate in this program.

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\* Staff Anesthesiologist, Department of Anesthesiology, Maine Medical Center, Portland, Maine.

† Staff Anesthesiologist, Department of Anesthesiology, Maine Medical Center, Portland, Maine; and Clinical Associate Professor, University of Vermont College of Medicine, Burlington, Vermont.

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Address reprint requests to Dr. Taenzer: c/o Kristen Sullivan, Department of Anesthesiology, Maine Medical Center, 22 Bramhall Street, Portland, Maine 04102. Address electronic mail to: ataenzer@maine.rr.com

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### *Surgical Technique*

The ACLR was performed using a bone-patellar tendon-bone autograft by one of three orthopedic surgeons. The bone-patellar tendon-bone graft was collected through a vertical anterior midline incision. The remainder of the procedure, including concomitant meniscectomy or meniscal repair (if necessary), was performed arthroscopically. Meniscal repairs were facilitated with auxiliary posterior incisions. The graft was secured with interference screws adjacent to the bone blocks in the femur as well as tibia. After completion of all appropriate intraarticular surgery, the defect in the patellar tendon was closed with sutures, and the patellar bone block collection site was packed with cancellous autogenous bone graft. Drains were placed in the joint and subcutaneous space before closing. A tourniquet was used during the entire procedure and was released after application of the dressings. A Cryo-Cuff (Air Cast, Summit, NJ), which was applied immediately after the procedure, was used for intermittent topical cryotherapy and compression for the 5-day study period. Intermittent passive range of motion was begun in the recovery room using a continuous passive motion device (Kinetic; Smith and Nephew Richard, Memphis, TN) and continued for 2-h periods three times a day for 5 days.

### *Anesthetic Technique*

Each patient received general anesthesia in a standardized fashion by one of nine anesthesiologists. Premedication and intraoperative opioids were routinely omitted. Anesthesia was induced with propofol and maintained with isoflurane and nitrous oxide. Muscle relaxation and intubation were performed at the discretion of the anesthesiologist.

### *Pain Management*

Patients without contraindication to acetaminophen or nonsteroidal anti-inflammatory agents were asked to take acetaminophen (650 mg) and ibuprofen (600 mg) orally four times a day, beginning the morning before the operation. Ketorolac was given intravenously before tourniquet inflation to all appropriate patients who did not receive ibuprofen preoperatively. Before the incision was made, 0.25 ml/kg of 0.25% bupivacaine with epinephrine (5 µg/ml) was injected subcutaneously at the expected puncture and incision sites. An additional 0.25 ml/kg of 0.25% bupivacaine was injected intraarticularly at the same time. These injections were repeated with the same dosage just before the release of the tourniquet. Thus, the total dose of bupivacaine with

epinephrine was 2.5 mg/kg. A pneumatic Cryo-Cuff was applied immediately after the procedure. In the postanesthesia care unit (PACU), patients with severe pain (defined as visual analog scale [VAS] of  $\geq 5$ ) were given intravenous fentanyl. All others were allowed 5–10 mg oxycodone tablets by mouth as needed. After discharge, patients were instructed to take acetaminophen (650 mg) with either ketorolac (10 mg) or ibuprofen (600 mg) by mouth four times a day for 5 days. Patients were instructed to take 5–10 mg oxycodone every 2 h if they experienced any pain at rest or more than minimal pain with activity.

### *Pain Measurement*

All patients were instructed before surgery on the use of an 11-point box scale, a type of VAS. The advantages of this scale have been previously described.<sup>7</sup> A verbal VAS was obtained at arrival to and at discharge from the PACU. The frequency and dose of fentanyl requirements were recorded. After discharge, patients were asked to complete box scales while at rest and after attempting straight leg-raising maneuver (SLRM) on awakening on each of the first 5 postoperative mornings. The maneuver was considered successful if the foot was elevated off the bed. In addition, patients were asked to record the number of oxycodone tablets they consumed on each of these 5 postoperative days (PODs). Questionnaires requesting this information were returned at the 1-week postoperative visit.

### *Straight Leg-raising Maneuver*

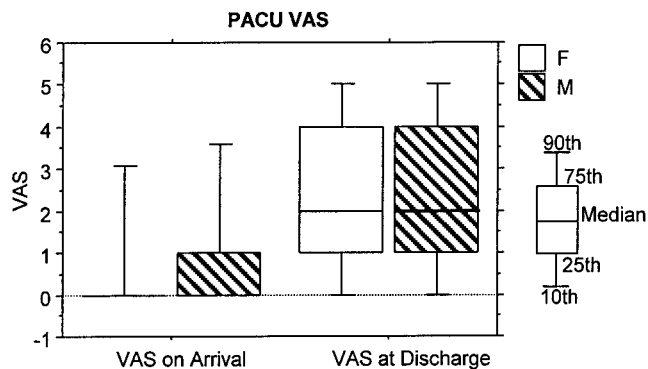
The SLRM was chosen as a measurement for postoperative assessment of activity-related pain because it is reproducible and easily interpreted maneuver that elicits pain. It is also a functionally important milestone after ACLR as it is a measure of quadriceps function, which is a necessary element for ambulation.<sup>8</sup>

### *Statistical Analysis*

All available data were plotted and analyzed for presence of normal distribution. Continuously distributed parametric variables are expressed as mean  $\pm$  SD and were tested with the Student *t* test. Nonparametric variables are expressed as medians and tested with the Mann-Whitney test. Dichotomous variables are expressed as proportions and tested with the chi-square test.

## **Results**

Of the 736 patients who underwent surgery, 186 women and 230 men completed surveys. Patients com-

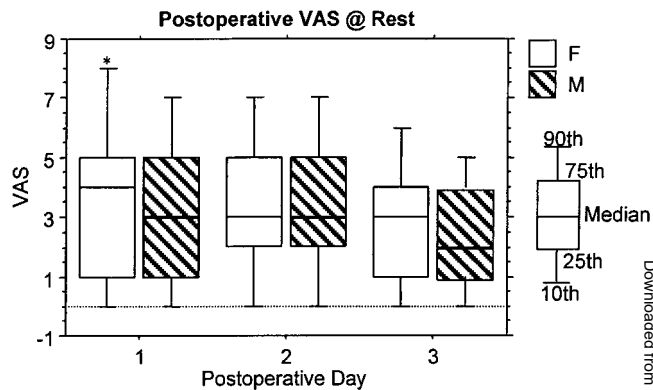


**Fig. 1.** Comparison of male and female visual analog scale (VAS) in the postanesthesia care unit (PACU). Median VAS for men and women at arrival to the PACU were 0 (range, 0–10) and 0 (range, 0–8), respectively. Median VAS for men and women at discharge from the PACU were 2 (range, 0–10) and 2 (range, 0–8), respectively.

pleting surveys decreased from 61% on POD 1 to 57% by POD 5. Slightly more women than men completed surveys, with a range from 64% *versus* 57% on POD 1 to 59% *versus* 55% on POD 5 (not statistically significant). Only patients completing surveys through POD 5 are included in the results. The mean age of patients completing surveys was  $27.6 \pm 10.0$  yr (women,  $25.8 \pm 10.6$  yr; men,  $29.1 \pm 9.2$  yr;  $P$  value for men *vs.* women = 0.009). These age demographics were not statistically different from those of the total 736 patients who underwent surgery. There was no difference in ratio of men to women between the operating surgeons. Pain scores and impaired function as measured by SLRM were maximal by day 2. As statistically significant differences between genders were found only on PODs 1 and 2, only data through POD 3 are displayed in the figures.

The immediate postoperative evaluation in the PACU in either VAS (fig. 1) or the proportion requesting fentanyl (33.4% women, 34.9% men;  $P = 0.68$ ) did not reveal differences between the genders. Fentanyl used in the PACU was not different between men and women ( $0.88 \pm 0.52$   $\mu\text{g/kg}$  *vs.*  $0.96 \pm 0.57$   $\mu\text{g/kg}$ ;  $P = 0.25$ ). There was a trend for women to spend more time in the PACU ( $80.9 \pm 1.7$  min *vs.*  $76.6 \pm 1.4$  min for men;  $P = 0.05$ ).

In comparing patients who completed postoperative surveys as one group and patients who did not complete surveys as another group, there was no difference between men and women in PACU pain scores within either group. In contrast, the patients not completing surveys had higher PACU predischARGE pain scores than those completing surveys: 2.9 *vs.* 2.5 both for men ( $P = 0.03$ ) and women ( $P = 0.02$ ).

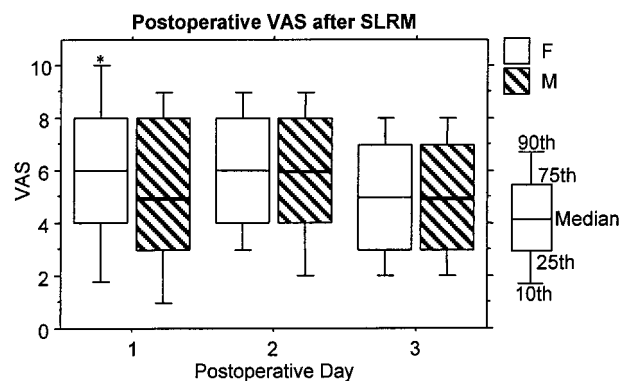


**Fig. 2.** Comparison of male and female visual analog scale (VAS) at rest, postoperative days 1–3. Median VAS for men and women on day 1 were 3 (range, 0–10) and 4 (range, 0–10), respectively. Median VAS for men and women on day 2 were both 3 (range, 0–10). Median VAS for men and women on day 3 were 2 (range, 0–9) and 3 (range, 0–9), respectively. \* $P < 0.05$ , men *versus* women.

Women reported statistically significant higher postoperative pain scores for pain at rest (fig. 2) on POD 1 ( $P = 0.04$ ) and for the pain scores after performing the SLRM (fig. 3) on POD 1 ( $P = 0.04$ ), but not on other days.

More women reported being unable to perform the SLRM compared with men, reaching statistical significance for POD 1 ( $P = 0.006$ ) and POD 2 ( $P = 0.006$ ; fig. 4).

There was no significant difference in consumption of oxycodone between the genders (POD 1 median for women and men = 2,  $P = 0.20$ ; POD 2 median for women and men = 3,  $P = 0.44$ ; POD 3 median for women and men = 2,  $P = 0.94$ ).



**Fig. 3.** Comparison of male and female visual analog scale (VAS) after straight leg-raising maneuver (SLRM), postoperative days 1–3. Median VAS for men and women on day 1 were 5 (range, 0–10) and 6 (range, 0–10), respectively. Median VAS for men and women on day 2 were both 6 (range, 0–10). Median VAS for men and women on day 3 were both 5 (range, 0–10). \* $P < 0.05$ , men *versus* women.

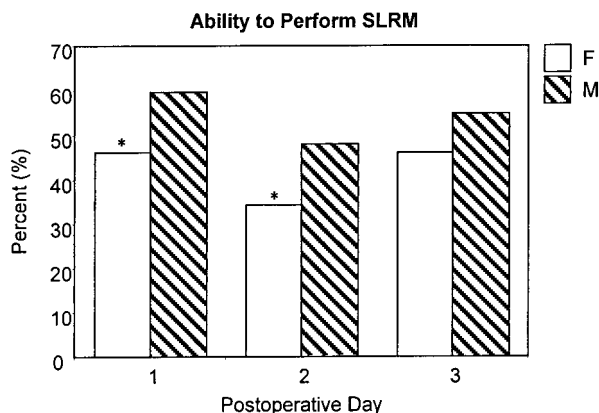


Fig. 4. Comparison of male and female ability to perform straight leg-raising maneuver (SLRM), postoperative days 1–3. On day 1, 46.2% of women *versus* 59.7% of men were able to perform an SLRM. On day 2, 34.4% of women *versus* 48.0% of men were able to perform an SLRM. On day 3, 46.1% of women *versus* 54.8% of men were able to perform an SLRM. \* $P < 0.05$ , men *versus* women.

## Discussion

Both men and women reported pain scores at rest and with activity that peaked on the second POD. These scores and their time course are consistent with those reported previously.<sup>6,9</sup> The magnitude of the scores is consistent with those previously associated with ratings of moderate or greater intensity.<sup>10</sup>

Women reported significantly higher pain scores at rest and with activity on POD 1 and decreased ability to perform SLRM on both PODs 1 and 2. Although the absolute difference in pain scores was not large, the association of a decrease in function with the increase in pain scores supports the clinical relevance of the differences in pain scores. An important clinical consequence of pain is impaired musculoskeletal function.<sup>11</sup> Earlier ability to mobilize the knee after surgery may limit or prevent deleterious effects of the operation and joint immobilization, such as intraarticular adhesions, articular cartilage trophic changes, and muscle atrophy.<sup>12,13</sup> The apparent decreased function observed with women may imply a higher risk of these complications for women compared with men.

Possible explanations for the differences in pain ratings and function include gender-related factors in effectiveness of analgesics, behavioral patterns, or neuroprocessing.

The analgesic regimen used in these patients involved four analgesics (acetaminophen, bupivacaine, ibuprofen

or ketorolac, and oxycodone), which, except for acetaminophen, have been shown to provide greater pain relief among men. It is therefore possible that the gender-related differences in pain scores are the result of gender-related differences in analgesia effectiveness.

Gender-related differences in responsiveness to non-steroidal anti-inflammatory drugs have been demonstrated.<sup>1</sup> As our patients all received either ibuprofen or ketorolac as part of our multimodal analgesic regimen, any gender-related difference in response to these analgesics might result in a gender-related difference in the pain experience after this procedure.

The majority of studies reporting on the gender-related responsiveness to opioids found a greater analgesic response among men in both animal and human models, likely because of greater  $\mu$ - and  $\kappa$ -opiate receptor-mediated analgesia.<sup>14–16</sup> It is thus conceivable that oxycodone, as part of our analgesic regimen, had a lesser effect on pain relief among women.

Other investigators have shown greater pain relief from local anesthetics in men compared with women in both experimental<sup>17</sup> and clinical<sup>18</sup> settings. Several studies have further shown that intraoperative local anesthetic infiltration may have prolonged effects on pain well beyond the period of expected neural blockade.<sup>19–21</sup> Although our data showed no immediate gender-related difference in pain perception in the PACU, a prolonged analgesic effect from the intraoperative local anesthetic beyond the anticipated immediate period of effectiveness may partly explain the differences in pain scores on POD 1.

Women might report different pain scores because of behavioral patterns.<sup>20,21</sup> One study found that the gender of the investigator influenced pain reports of men such that they reported lower pain scores to a female investigator.<sup>22</sup> Several studies are inconclusive and contradictory in addressing whether differences in pain perception between the genders are related to differences in willingness to report pain.<sup>21–24</sup> Other studies using involuntary measures such as pupil dilation or activation of the prefrontal cortex suggest that neuroprocessing of noxious stimuli is heightened in women compared with men.<sup>25,26</sup> Data in the present study were collected by a daily report written by each patient and collected by office staff at a postoperative appointment. The lack of reporting of postdischarge data to any member of the team, either male or female, should minimize potential reporting bias.



There are a number of potentially confounding variables in this study and limits to the strength with which we can interpret our results. Although the data were gathered prospectively, it was retrospectively analyzed. This, in combination with the low rate of survey return, weakens the strength of our conclusions. Although the rate of survey return was close between men and women, more women did complete the survey. Any difference in how patients with more or less pain or ability to perform the SLRM might be inclined to complete the survey would potentially confound our results. A subtle difference that might not affect the results of a study with a high rate of survey return could affect our results with our approximately 40% noncompliance in survey completion. That patients completing surveys had less pain before discharge from the PACU and that more women completed surveys suggests, if anything, a tendency to strengthen our results. However, it is difficult to extrapolate this PACU data on all patients to the experience on POD 1 and beyond of the patients not completing the survey. A prospective study with safeguards to ensure a survey return near 100% would address these problems.

An effect of age on pain and ability to form the SLRM could also confound the results given the difference in age between men and women. However, this is unlikely because the small mean difference of 3.3 yr between men and women in our study population, although statistically significant, is probably clinically irrelevant.

To date there have been no studies that have examined the functional relevance of gender-related differences in experience of postoperative pain. This is the first time that higher pain scores among women have been shown to be associated with a measurable decrease in postoperative function. Our findings are strengthened by the size of the studied population and the consistent nature of trauma inherent in a study of a single type of operation. The use of the SLRM as a functional outcome may or may not be a valid proxy for more practical outcomes, such as return to full work capacity or the incidence of complications caused by immobility. Future studies should address a broader and more clinically relevant set of functional outcomes. This study with its limitations does not allow us to draw firm conclusions but does suggest the link between gender and pain and function. Future work should explore this association. Furthermore, the differences found in this study suggest that all future studies of pain should control carefully for the potential for gender-related bias in pain reports.

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## GENDER AFFECTS REPORT OF PAIN AND FUNCTION AFTER ACL SURGERY

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