The impact of the learning curve on adhesion formation in a laparoscopic mouse model

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Objective: To evaluate the impact of surgeon training on adhesion formation in a laparoscopic mouse model. Laparoscopic surgery and bowel manipulation was demonstrated to enhance postoperative adhesion formation.
Design: Prospective randomized, controlled trial.
Setting: University laboratory research center.
Animal(s): 200 BALB/c and 200 Swiss female mice.
Intervention(s): Adhesions were induced by opposing bipolar lesions and 60 minutes of pneumoperitoneum. Each surgeon operated on 80 mice (40 Swiss and 40 BALB/c), the only variable thus being his/her increasing experience. Some surgeons were already experienced gynecologists, others were starting their training.
Main Outcome Measure(s): End points were the duration of surgery while performing the lesions. The adhesion formation was scored quantitatively (proportion and total) and qualitatively (extent, type, and tenacity) after 7 days.
Result(s): With training, duration of surgery and adhesion formation decreased exponentially for all surgeons, whether experienced or not. Experienced surgeons had initially a shorter duration of surgery, less adhesion formation, and less de novo adhesions than inexperienced surgeons.
Conclusion(s): These data suggest that laparoscopic skills improve with training, leading to a decrease in the duration of surgery and formation of adhesions. Therefore completion of a standardized learning curve should be mandatory when initiating adhesion formation studies both in laboratory or clinical setting. (Fertil Steril® 2011;96: 193–7. ©2011 by American Society for Reproductive Medicine.)

Key Words: Learning curve, laparoscopy, adhesions, mouse model, training, surgery

Surgical training has always been an essential part in the residency of the young surgeon. Since the introduction of laparoscopic surgery, learning curves are frequently used to analyze the effect of training and to assess the competency of surgeons. This can be done, without any risk for the patient (1), thanks to the development of different methods of laparoscopic surgical training, such as live and cadaver animal training, human cadaver training, box trainer, video trainer, and virtual reality training by computer simulation (2). Learning curves are different for different type of surgery and surgeons can be experienced in one procedure and not in another (3–5).

Learning curves in endoscopic surgery, as reported in the literature, showed that they always improve outcomes in different surgical procedures (2, 6–11) and after a rapid improvement in skills at the beginning, which varies with the skills investigated (tying, suturing, cutting, dissecting, lifting, grasping, and transferring objects with both hands) (12), a plateau is reached (i.e., knot tying is learned much quicker than stitching) (13). Learning curves are reflected in a progressively decreasing operating time, an enhanced precision, and a decrease in complications (6, 7, 14). Specifically, the duration of surgery (14–19) and complication rate (18, 19) is significantly lower for experienced surgeons compared with junior ones (14), with an important impact on costs (20, 21).

The impact of learning curves on experiments involving animal models has rarely been investigated (14). This might be especially important in experiments investigating postoperative adhesion formation, as adhesion formation has been shown to decrease with a shorter duration of surgery (22) and with gentle tissue handling (23, 24). Good surgical techniques is widely believed to decrease postoperative adhesions.

During the past years our group developed and validated a strictly standardized laparoscopic mouse model for the study of postoperative adhesion formation and tumor implantation. To investigate the minimum experience required to perform experiments we prospectively investigated the learning curves and the impact of training on the extent and the variability of postoperative adhesion formation, as well as the effect on operating time.

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MATERIALS AND METHODS

The Laparoscopic Mouse Model for Adhesion Formation

The experimental setup (i.e., animals, anesthesia and ventilation, laparoscopic surgery and induction, and scoring of peritoneal adhesions) has been described in detail previously (22–31). Briefly, the model consisted of performing bipolar lesions during laparoscopy followed by 60 minutes of pure CO_2 pneumoperitoneum. The pneumoperitoneum was induced using the Thermoflator (Karl

Storz) through a 2-mm endoscope with a 3.3 external sheath for insufflation (Karl Storz) introduced into the abdominal cavity through a midline incision caudal to the xyphoid appendix. The incision was closed gas tight around the endoscope to avoid leakage. The insufflation pressure was 15 mm Hg and humidified gas (Humidifier 204320 33; Karl Storz) was used. After the establishment of the pneumoperitoneum, two 14-gauge catheters (Insyte-W, Vialon; Becton Dickinson) were inserted under laparoscopic vision. Standardized 10- $\times$ 1.6-mm lesions were performed in the antimesenteric border of both right and left uterine horns and in both the right and left pelvic side walls with bipolar coagulation (20 W, standard coagulation mode, Autocon 350; Karl Storz). Because anesthesia and ventilation influence body temperature (28), the timing between anesthesia (T0), intubation (at 10 minutes, T10), and the onset of the experiment (at 20 minutes, T20) was strictly controlled. After 7 days, adhesions were scored quantitatively (proportion and total) and qualitatively (extent, type, tenacity) blindly during laparotomy under a stereomicroscope. The entire abdominal cavity was visualized using a xyphopubic midline and a bilateral subcostal incision. After the evaluation of ports sites and viscera (omentum, large and small bowels) for de novo adhesions, the fat tissue surrounding the uterus was carefully removed. The length of the visceral and parietal lesions and adhesions were measured. Adhesions, when present, were carefully lysed to evaluate their type and tenacity. The terminology of Pouly and Seak-San (32) was used, describing de novo adhesion formation for the adhesions formed at nonsurgical sites and adhesion formation for adhesions formed at the surgical site.

Animals

The present study was performed in 400, 12–13-week-old female mice (i.e., 200 BALB/cJ@Rj mice; inbred strain) weighting 20–30 g and 200 Swiss mice (outbred strain) weighting 30–40 g. Animals were kept under standard laboratory conditions and diet at the animal facilities of the Katholieke Universiteit Leuven. The study was approved by the Institutional Review Animal Care Committee of the Katholieke Universiteit Leuven.

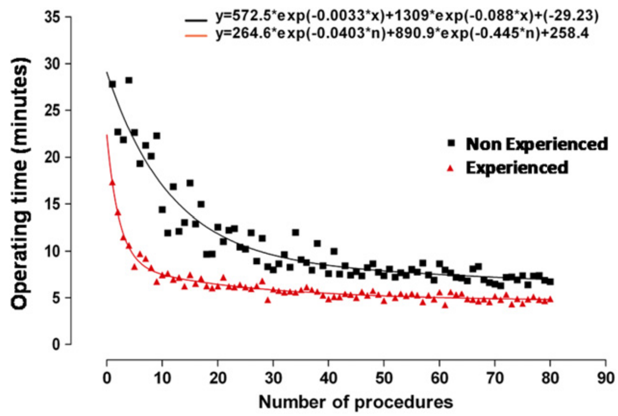
Experimental Design and Surgical Procedures

The experiment was designed to evaluate the effect of training, assessed by the consecutive surgeries, on operating time and on the extent and variability of postoperative adhesion formation. The operating time was measured from T20 (i.e., from the beginning of surgery, exactly 20 minutes after induction of anesthesia) until the end of the procedure with the removal of catheters for instrumentation and port sites closure. In addition, the codes of intervention order were broken only at the end of the training experiment. Each trainee performed sequentially 80 interventions to induce adhesion formations. All trainees were inexperienced for the laparoscopic procedure in a mouse model, but some of them were experienced gynecologists after their training in gynecology (3 trainees), whereas other surgeons were inexperienced at the end of medical school (2 trainees).

All experiments were performed using block randomization by days. Therefore, a block of animals comprising one animal of each strain, one BALB/c mouse and one Swiss mouse were always operated in a single session on the same day to avoid day-to-day variability. In addition, within a block, experiments were performed in random order. Before surgical procedure initial body temperature and weight were measured.

FIGURE 1

Duration of surgery during training. Learning curve expressed as duration of the surgery versus number of consecutive procedures for experienced (n = 3) and nonexperienced surgeons (n = 2). Dots represent the real operating times for each mouse. The lines were calculated from the individual operating times after a two-phase exponential decay model.



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Statistics

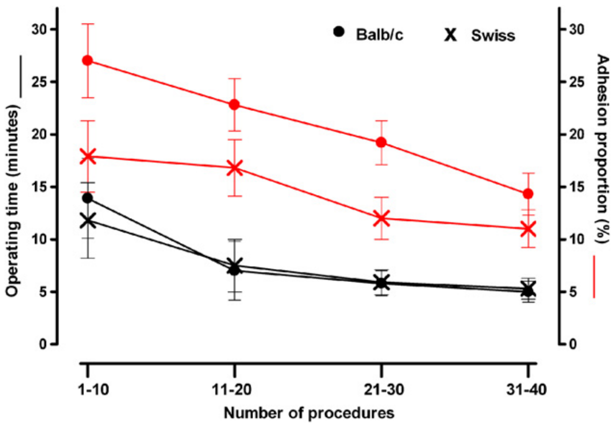
Statistical analyses were performed using GraphPad Prism version 4 (GraphPad Software Inc.). Multifactorial analyses were achieved with GLM and Logistic procedures using the SAS System (SAS Institute). The coefficient of variation (CV), a normalized measure of dispersion, was calculated as the ratio of the standard deviation to the mean multiplied by 100.

RESULTS

With training, assessed by consecutive surgeries, duration of surgery decreased exponentially in both groups, demonstrating a clear learning curve that can be described as a two-phase exponential decay model (nonexperienced: $R^2 = 0.72$; experienced: $R^2 = 0.73$) (Fig. 1). In BALB/c mice the real and calculated operating times for nonexperienced surgeons decreased from 19 $\pm$ 6 minutes and 22 $\pm$ 4 minutes for the first 10 procedures to 7 $\pm$ 1 minutes and 7 $\pm$ 1 minutes for the last 10 procedures (P=.0001; P=.0001, respectively). For experienced surgeons time decreased from 8 $\pm$ 1 minutes and 10 $\pm$ 3 minutes for the first 10 procedures to 4 $\pm$ 0.3 minutes and 4 $\pm$ 0.03 minutes for the last 10 procedures. In Swiss mice the real and calculated operating times from nonexperienced surgeons decreased from 17 $\pm$ 6 minutes and 22 $\pm$ 4 minutes for the first 10 procedures to 7 $\pm$ 1 minutes and 7 $\pm$ 1 minutes for the last 10 procedures (P=.0001; P=.0001, respectively). For experienced surgeons time decreased from 8 $\pm$ 3 minutes and 10 $\pm$ 3 minutes for the first 10 procedures to 4 $\pm$ 0.3 minutes and 5 $\pm$ 0.03 minutes for the last 10 procedures (P=.0001; P=.0001, respectively). As expected, the real and calculated operating times both for BALB/c and Swiss mice were not statistically different (t-test) both for the first 10 procedures and for the last 10 procedures. When the effects of training with time, the experience of the surgeon and the mouse strain were evaluated simultaneously using multifactorial analysis (proc GLM), we confirmed the importance of decreasing operating time (P=.0001) and the effect of experience

FIGURE 2

Duration of the surgery and adhesion formation during learning curve in different mouse strain. Duration of the surgery and adhesion formation during learning curves in BALB/c (n = 200) and Swiss mice (n = 200). Number of procedures were grouped by groups of 10 blocks (1 block = 2 procedures: 1 BALB/c + 1 Swiss). Mean and SD are indicated.



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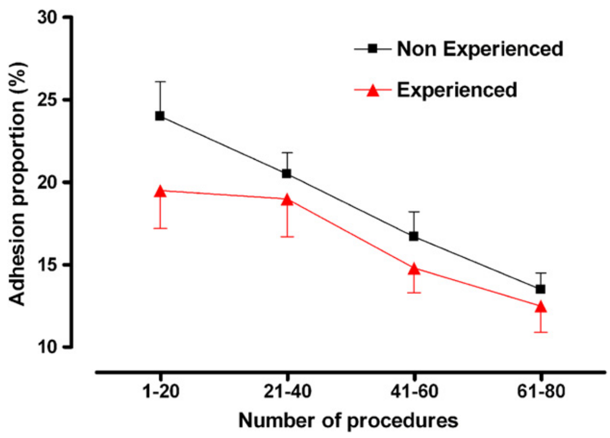
(P=.0001), whereas the mouse strain was not important as could be anticipated (P=not significant [NS]) (Fig. 2).

Similarly, the effects of training (expressed by the consecutive number of surgeries), operating time, experience, and mouse strain on adhesion formation were evaluated using multifactorial analysis (proc GLM) (Figs. 2 and 3). Adhesion formation was lower with the consecutive number of surgeries (proportion: P=.01; total: P=.01; extension: P=.02; type: P=.01; tenacity: P=006), for surgeries of shorter operating time (proportion: P=.02; total: P=.04; extension: P=.02; type: P=.02; tenacity: P=.04), among experienced surgeons (proportion: P<.0001; total: P=.04; extension: P=.001; type: P=.03; tenacity: P=.04), and in Swiss mice (P=NS) (Fig. 2).

FIGURE 3

Adhesion formation during learning curve. Adhesion formation expressed as proportion of adhesions versus number of consecutive procedures in both experienced (n = 3) and nonexperienced surgeons (n = 2). Mean and SD are indicated.



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It was decided arbitrarily to make four groups of 10 blocks (G1, block 1–10; G2, block 11–20; G3, block 21–30; G4, block 31–40). With this grouping, the interanimal variability for operating time and for adhesion formation was assessed using the CV. The CV of operating time among nonexperienced surgeons were 41%, 35%, 25%, and 20% for BALB/c mice and 39%, 40%, 22%, and 17% for Swiss mice for G1, G2, G3, and G4, respectively; among experienced surgeons were 45%, 24%, 20%, and 22% for BALB/c mice and 37%, 24%, 20%, and 21% for Swiss mice for G1, G2, G3, and G4, respectively. The CV of the proportion of adhesions were 62%, 48%, 54%, and 38% for BALB/c mice and 106%, 92%, 96%, and 77% for Swiss mice for G1, G2, G3, and G4, respectively. The effects of the consecutive number of surgeries, measured by groups, and of mouse strain on operating time and its CV and on the proportion of adhesions and its CV were evaluated with a multifactorial analysis (proc GLM). Both operating time and its CV decreased with the number of surgeries (P=.0001; P=.0001, respectively), whereas they were not affected by mouse strain (P=NS; P=NS, respectively). Both the proportion of adhesions and its CV decreased with the number of surgeries (P=.002; P=NS) and were affected by mouse strain (i.e., for BALB/c mice the proportion of adhesions was higher and the CV was lower).

DISCUSSION

To the best of our knowledge this is the first article aiming to study the effect of surgical training on postoperative adhesion formation in a laparoscopic mouse model. A previous study, performed in rabbits, showed that postoperative adhesion formation, duration of surgery, and complication rate decreased with surgeon training, expressed by the consecutive number of procedures performed (14, 33, 34).

In the present study, we compared two groups of surgeons (i.e., experienced and nonexperienced surgeons). Experienced surgeons not only started with lower duration of surgery but also achieved the plateau earlier (after 10 procedures), whereas nonexperienced surgeons started with longer duration of surgery and, although the duration decreased, it did not achieve the level of experienced surgeons even after 80 consecutive procedures. A less traumatic, more precise and gentle surgical technique gained with experience appears to be important as postoperative adhesion formation was lower already after the first 10 procedures within the group of experienced surgeons in comparison with nonexperienced surgeons, confirming the data of the effect of manipulation-enhanced adhesions (23). This difference among groups of surgeons decreased with the number of surgical procedures, underlining the importance of training. Our data confirm the well-known effect of training on the learning curve (6, 12, 13, 22, 25–28, 30, 35, 36). Gentle tissue handling, however, is more complex than is reflected in the duration of surgery, as for similar operating times, experienced surgeons had always less adhesions than inexperienced surgeons during the entire learning curve.

Postoperative adhesion formation is influenced not only by surgical training but also by the duration of the pneumoperitoneum, which in the present study was kept constant at 60 minutes. Less adhesion formation with shorter procedures may happen due to less exposure to CO_2 pneumoperitoneum and thus to less pneumoperitoneum-enhanced hypoxia, CO_2, and pH changes. In the study performed in rabbits, duration of surgery also seemed to be important in the outcome of postoperative adhesion formation, although it is difficult to completely separate both effects as duration of surgery and training of surgeon are intimately related.

Other reports studying only the effect of CO_2 or helium pneumoperitoneum on postoperative adhesion formation have shown an important effect of the time of exposure. Those studies show the same situation—the longer the exposure, the higher the adhesion formation (22, 37).

Our study indicates that genetic background could also influence adhesion formation, at least after laparoscopic surgery (38). BALB/c mice, an inbred strain, showed lower interanimal variability and higher adhesion formation (the latter not significant) in comparison with Swiss mice, an outbred strain, observation to take into account when developing a standardized animal model for the study of adhesion formation. Strain differences have been reported for other processes involving fibrosis and healing responses such as hepatic, lung, and colorectal fibrosis (39–41), myocardial and ear wound healing (42, 43), and bone regeneration (44). This is not surprising because inbred strains, maintained by sibling (brother × sister) mating for 20 or more generations, are genetically almost identical, homozygous at virtually all loci, and with high phenotypic uniformity (45). This less interanimal variability in inbred strains has been reported for many processes such as sleeping time under anesthesia (46).

The mouse model has many advantages compared with other animal models because it is relatively cheap, easy to handle, and does not require strict sterile conditions for surgery. Furthermore, it is particularly useful for diverse studies because of the availability of animals with low genetic variability (i.e., inbred mice), underexpressing or overexpressing specific genes (i.e., transgenic mice), and immunodeficient by spontaneous mutation (i.e., nude mice [T-cell deficient] and SCID mice [T&B cell deficient]). In addition, many specific mouse assays and monoclonal antibodies are available.

In conclusion, first, this study confirms that surgical training is extremely important, not only in a hospital setting when dealing with patients but also when performing surgical studies with the aim of analyzing the outcome. In this case, training experience has a marked effect on the development of postoperative adhesion formation. Second, it is preferable to use a strain with high adhesion formation potential and low interanimal variability such as BALB/c mice. We believe fewer inbred animals will be needed to achieve a given level of statistical precision than if outbred animals are used (44). It is, however, necessary to point out that inbred strains in general weigh less than outbred strains (average of 20 g vs. 32 g), which increases the technical skills required to do the experiments, especially those involving laparoscopic surgery.

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