Patient-centered modeling of dynamic postoperative pain trajectories

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Enhanced recovery after surgery (ERAS) concepts are well accepted and popular in today's perioperative medicine. It is a multimodal perioperative care protocol and has become an important focus of perioperative management now. Nonopioid postoperative pain control is one of the critical elements of ERAS protocols. A variety of nonopioid systemic medical therapies as well as epidural, regional, and neuraxial techniques have been described as improving pain control while reducing opioid use. Multimodal and preemptive analgesia facilitates early mobility and early return of bowel function and decreases postoperative morbidity.[1] The effect of epidural analgesia is well established, especially for labor, major open abdominal surgery and thoracotomy. However, other benefits of epidural analgesia, such as accelerated recovery and decreased postoperative complications, remain debated.[2]

Most pain studies focused on the comparisons of the effectiveness of a pain intervention among groups at a specific time point. Only the pain trajectory analyses try to explore longitudinal pain score data to investigate issues on the pain and analgesia. Pain trajectory analyses usually applied repeated measures analysis of variance (ANOVA) and linear mixed models to analyze serial changes in pain scores over time and treat differences among individuals as error variance, which may contain valuable information with increasing complexity. Few studies emphasize the pain trajectories after surgery in patients receiving epidural analgesia. In this issue of JCMA, Dr. Lee and her colleagues reported the findings from a retrospective study that evaluated the postoperative pain trajectories over time for the patient receiving patient-controlled epidural analgesia.[3] They enrolled 1294 patients with 6034 pain score observations for postoperative day 1 to 5. Other collected variables included gender, age, weight, height, body mass index, American Society of Anesthesiologists (ASA) physical status classification, total anesthesia time, infusion pump setting, and surgical site (chest, abdomen, and lower extremity). Latent curve analysis was used to develop a model which traced the changes in pain scores over time and investigate the influential factors of pain trajectories. The results show that female gender, longer anesthesia time, higher infusion rate, and lower extremity surgery were significantly associated with higher baseline pain scores. Patients undergoing chest surgery had lower baseline pain scores. Regarding the decreasing trends in pain trajectories, older age, ASA class ≥3, higher demand dose and infusion rate, and undergoing chest surgery were associated with slower pain resolution after surgery. In contrast, faster pain resolution was noted in patients with higher body weight. Limitations of this study included impossibility to evaluate the effects of unobserved variables on pain trajectories due to the retrospective study design and limited classification of surgery. Strength included the development of a prediction model and integration with postoperative infusion pump settings.

Latent curve analysis is a new method to explore both inter- and intraindividual variability in growth trajectories.[4] It is an essential and influential statistical method mainly used in social and behavioral sciences. However, this statistical method could facilitate research pertaining to clinical medicine. For example, the evolving clinical course of a disease, the effect of chronical medical treatment, and the outcome prediction for each individual patient, all involve longitudinal data analysis. Latent curve analysis makes more elaborate use of time information than traditional statistical methods. Due to medical ethics or constrained resources, we may have to investigate the causal relationship via observational data. In this circumstance, latent curve analysis may provide a solid temporal relationship. In addition, the handling of individual trajectories and the overall mean trajectory is appropriate to the nature of interindividual variations. Recently some researchers also applied latent curve analysis in the field of chronic pain management. The clinicians can use latent curve models to predict disability in arthritis, chronic postsurgical pain, and low back pain.[5–7] Chang and colleagues have series of studies which focused on predicting postoperative pain trajectories, including both pain severity and pain scores decreasing trends since 2013. Postoperative epidural analgesia demand, intravenous analgesics consumption, and pain trajectories after total knee arthroplasty and colorectal surgery were predicted with latent curve models.[8–10] Tai et al also conducted a latent curve analysis study with a total of 3376 patients and 20 838 pain score observations after intravenous patient-controlled analgesia. The study revealed females and longer anesthesia time increased the baseline level of pain, whereas older age, ASA class ≥3, and longer anesthesia time decrease the trend of pain resolution.[11]

Several other prior studies and reviews have proposed different preoperative predictors of postoperative pain. Kalkman et al[12] developed and validated a prediction rule for early

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postoperative severe pain in surgical inpatients, using predictors as female gender, age, preoperative pain, type of surgery, anxiety, and incision size. A cohort of surgical inpatients of 1416 undergoing various procedures except for cardiac surgery and intracranial neurosurgery in a University Hospital were studied to develop the rule. Ip et al disclosed a systemic review, including 48 eligible studies with 23 037 patients. The result identified four significant predictors for postoperative pain: preoperative pain, anxiety, age, and type of surgery.[13] Yang et al made a systemic review enrolled in 33 studies with 53 362 patients and they identified nine risk factors for predicting postoperative pain: age, female, smoking, depression, anxiety, sleeping difficulties, high body mass index (BMI), preoperative pain, and preoperative analgesics.[14] Most studies have consensus on risk factors of postoperative pain, including preoperative pain, anxiety, female, and type of surgery, and agree with findings of this study. However, the role of age, body weight, anesthesia time, and ASA class status on postoperative pain remains controversial. As a result, inconsistent findings in different studies make acute pain management a challenge for clinicians.

Postoperative epidural analgesia with local anesthetics may play a role in the era of ERAS. The results of the clinical trial by Lee et al in the current issue of JCMA added to the cumulative evidence of accurate prediction of acute postoperative pain. Both pain intensity and pain resolution can be predicted using latent curve models. Latent curve analysis provided insights into the variations in postoperative pain trajectories over time. The prediction model has the potential to be integrated with real intervention data and facilitate real-time and effective pain management tailored to individual needs. We expect that statistical methods such as latent curve analysis revealed more insight into the ubiquitous longitudinal medical data. Before this, researchers need more suggestions to choose a train of relevant parameters, such as the sampling size, the growth model, the residual structure, to garner the power of latent curve analysis. More researches in the topics might fill the void of knowledge to pave a path toward precision medicine.

REFERENCES

1. Ljungqvist O, Scott M, Fearon KC. Enhanced recovery after surgery: a review. *JAMA Surg* 2017;**152**:292–8.
2. Bos EME, Hollmann MW, Lirk P. Safety and efficacy of epidural analgesia. *Curr Opin Anaesthesiol* 2017;**30**:736–42.
3. Lee MY, Chang WK, Wu HL, Lin SP, Tsou MY, Chang KY. Dynamic analysis of variations in postoperative pain trajectories over time in patients receiving epidural analgesia using latent curve models. *J Chin Med Assoc* 2020;**83**:89–94.
4. Duncan TE, Duncan SC. The ABC'S of LGM: an introductory guide to latent variable growth curve modeling. *Soc Personal Psychol Compass* 2009;**3**:979–91.
5. James RJE, Walsh DA, Ferguson E. Trajectories of pain predict disabilities affecting daily living in arthritis. *Br J Health Psychol* 2019;**24**:485–96.
6. Chen Y, Campbell P, Strauss VY, Foster NE, Jordan KP, Dunn KM. Trajectories and predictors of the long-term course of low back pain: cohort study with 5-year follow-up. *Pain* 2018;**159**:252–60.
7. Althaus A, Arránz Becker O, Moser KH, Lux EA, Weber F, Neugebauer E, et al. Postoperative pain trajectories and pain chronification: an empirical typology of pain patients. *Pain Med* 2018;**19**:2536–45.
8. Chao PW, Lin SP, Tsou MY, Kuo IT, Chang KY. Assessing the impact of renal function on trajectory of intravenous patient-controlled analgesic demands over time after open and laparoscopic colorectal surgery using latent curve analysis. *Clin J Pain* 2016;**32**:695–701.
9. Lo PH, Tsou MY, Chang KY. Modeling the trajectory of analgesic demand over time after total knee arthroplasty using the latent curve analysis. *Clin J Pain* 2015;**31**:776–81.
10. Hu KH, Tsou MY, Chan KH, Chang KY. An investigation on influential factors of patient-controlled epidural analgesic requirement over time for upper abdominal surgeries. *J Chin Med Assoc* 2013;**76**:446–51.
11. Tai YH, Wu HL, Lin SP, Tsou MY, Chang KY. Influential factors of postoperative pain trajectories in patients receiving intravenous patient-controlled analgesia: a single-centre cohort study in Taiwan. *BMJ Open* 2019;**9**:e031936.
12. Kalkman CJ, Visser K, Moen J, Bonsel GJ, Grobbee DE, Moons KG. Preoperative prediction of severe postoperative pain. *Pain* 2003;**105**:415–23.
13. Ip HY, Abrishami A, Peng PW, Wong J, Chung F. Predictors of postoperative pain and analgesic consumption: a qualitative systematic review. *Anesthesiology* 2009;**111**:657–77.
14. Yang MMH, Hartley RL, Leung AA, Ronksley PE, Jetté N, Casha S, et al. Preoperative predictors of poor acute postoperative pain control: a systematic review and meta-analysis. *BMJ Open* 2019;**9**:e025091.