Analgesic Monitoring Indices in Response to Noxious Stimuli of Laparoscopic Cystectomy Surgery and Their Time Optimization

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Introduction: Adequate pain relief is a sophisticated work for perioperative patient management. Parameters, based on different physiological data, including heart rate, autonomic nervous system and electroencephalographic (EEG) activity are developed to reflect dynamic changes of noxious stimuli in surgery. However, the duration from the painful stimulus to the peak index of these parameters are not elucidated. Several factors are involved, such as the physiologic response time and the time window of data processing in the instrument. The knowledge of such time profiles of parameters for pain may help the anesthesiologist to assess the analgesia-nociception balance more accurately.
In this study, we investigate the time profile of indices from several analgesic monitoring instruments in response to uniform noxious stimuli. The precise time points facilitate the subsequent probing of the best time duration of index responses in terms of the group receiver operating characteristic (ROC) area.

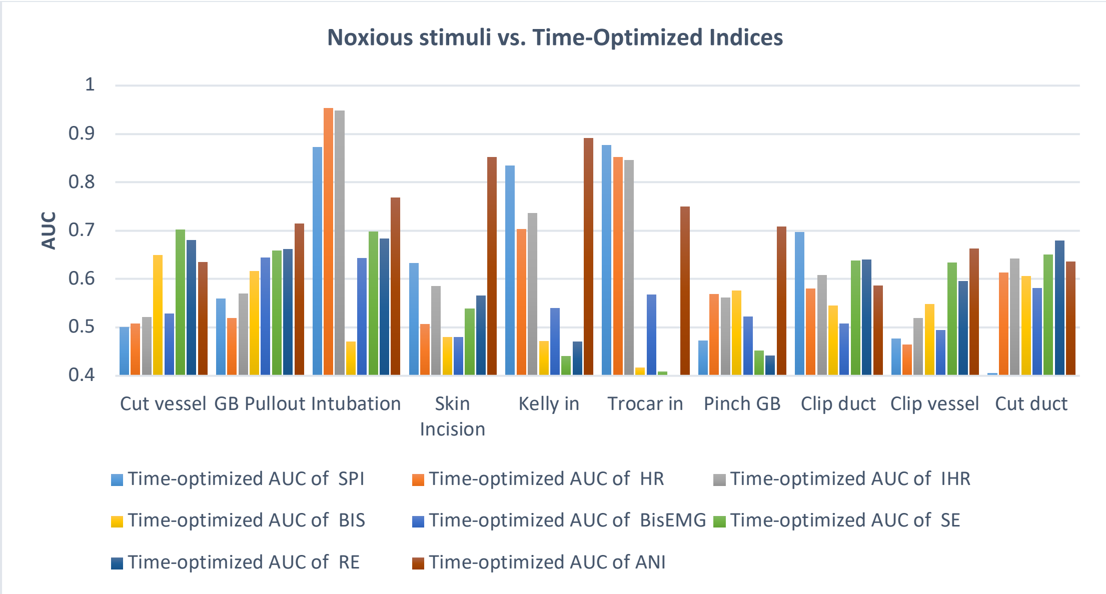
Methods: After obtaining institutional ethic committee approval, we conducted the prospective observation study to collect intraoperative data from the monitoring instrument from patient undergoing laparoscopic cholecystectomy surgery with each informed consent. EEG monitoring instruments including Bispectral Index (BIS), Entropy module (Spectral Entropy and Response Entropy), Analgesia Nociception Index (ANI), and Surgical Pleth Index (SPI) as well as the standard patient monitor (GE CARESCAPE B850, GE Healthcare, Chicago, IL) were attached with corresponding sensors per clinical standard and manufacturers' instructions. The data were recording for offline analysis. We recorded the exact time stamps of sequential noxious stimuli, including endotracheal intubation, skin incision, peritoneal penetration via Kelly hemostatic forceps, laparoscopic trocar tube insertion, ballbladder pinch, cystic duct clamping, cystic duct cutting, cystic vessel clamping, cystic vessel cutting.

The data analysis is performed with respect to the stimulus time to find the "best" time interval after. With respect to each stimulus, we use the one minute before as the "pre-stimulus" period and the subsequent two minutes as the interval to search for the "optimal" post-stimulus period. After normalizing data of "potential" post-stimulus period by the mean value of pre-stimulus period with respect to each case and index, we use the group area under the ROC curve (AUC) as the fitness function to obtain the optimal post-stimulus period. Data between 10% and 90% percentile were considered for calculation. The analysis was performed by R language (ver. 4.0.3) and the R package *pROC* (ver. 1.16.2).

Results: SPI and ANI are the best two noxious indices across all noxious stimuli except the endotracheal intubation. The time optimization shows stronger responses in somatic area than visceral area, while the pinch of gallbladder and the cystic duct clipping are the most two visceral stimuli according to SPI and ANI index. The maximum response time of SPI (73.5s) is earlier than that of ANI (100.0s). EEG derived indices are relatively obtuse.

Conclusions: The strengths and time profiles of indices are distinct and probably valuable for Intraoperative analgesics administration.

Figure:



Noxious stimuli vs. Time-Optimized Indices
AUC
1
0.9
0.8
0.7
0.6
0.5
0.4
Cut vessel
GB Pullout
Intubation
Skin Incision
Kelly in
Trocar in
Pinch GB
Clip duct
Clip vessel
Cut duct
Time-optimized AUC of SPI
Time-optimized AUC of HR
Time-optimized AUC of IHR
Time-optimized AUC of BIS
Time-optimized AUC of BisEMG
Time-optimized AUC of SE
Time-optimized AUC of RE
Time-optimized AUC of ANI