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The influence of anesthesia on heart rate complexity during elective and urgent surgery in 128 patients

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ABSTRACT

Background: As an emerging "new vital sign," heart rate complexity (by sample entropy [SampEn]) has been shown to be a useful trauma triage tool by predicting occult physiologic compromise and need for life-saving interventions. Sample entropy may be confounded by anesthesia possibly limiting its value intraoperatively. We investigated the effects of anesthesia on SampEn during elective and urgent surgical procedures. We hypothesized that SampEn is reduced by general anesthesia.

Methods: With institutional review board–approved waiver of informed consent, 128 patients undergoing elective or urgent general surgery were prospectively enrolled. Real-time heart rate complexity was calculated using SampEn through electrocardiogram recordings of 200 consecutive beats in a continuous sliding-window fashion. We recorded SampEn starting 10 minutes before induction until 10 minutes after emergence from anesthesia. The time before induction of anesthesia was categorized as period 1, the time after induction and before emergence as period 2 (intraoperative), and the time after emergence as period 3. We analyzed SampEn changes as patients moved between the different periods and made 3 comparisons: from period 1 with period 2 (comparison A), from period 2 with period 3 (comparison B). We also compared period 1 with period 3 SampEn (comparison C).

Results: The mean SampEn value for all patients before induction of anesthesia was 1.55 ± 0.58. In each 1 of the 3, comparisons there was a decline in SampEn. Comparison A had a mean decrease of 0.53 ± 0.55 ($P < .0001$), comparison B had a decrease of 0.13 ± 0.52 ($P < .0051$), and the mean SampEn difference for comparison C was 0.66 ± 0.53 ($P < .0001$). Certain pharmacologics had significant effect on SampEn as did need for urgent surgery and American Society of Anesthesiologists class.

Conclusion: Sample entropy decreases after induction of anesthesia and continues to decrease even immediately after emergence in patients without any immediately life-threatening conditions. This finding may complicate interpretation low complexity as a predictor of life-saving interventions in patients in the perioperative period.

1. Background

Heart rate variability ([HRV], measured by a variety of techniques including time and frequency domain calculations) and complexity have frequently been described as a "new vital sign" because traditional vital signs are unreliable predictors of severity of injury after trauma, when the compensatory mechanisms are yet to be exhausted [1-12]. Cardiac complexity quantified via sample entropy (SampEn) measures the degree of irregularity in this signal with improved predictive functions over traditional HRV for trauma patients [11-13]. Low complexity, or increased regularity, is indicative of an altered autonomic-humeral response and adaptation, or perhaps maladaptation, to physiologic stress [5,9-11,13]. Decreased complexity has been associated with mortality and predicting the need for life-saving interventions in trauma patients [5,9,10].

Decreases in HRV during anesthesia have previously been demonstrated [14-17]. In patients undergoing general anesthesia, HRV has been proposed to evaluate the function of the autonomic nervous system [18]. In addition, HRV may be used to monitor nociception, depth of anesthesia, predict the risk of hypotension development during general anesthesia, and may have prognostic and diagnostic values for perioperative risk stratification [15,19-21]. The effect of anesthesia on SampEn, however, remains largely uncharacterized, particularly when usng short data set SampEn analysis [22].

We aimed to prospectively measure SampEn in real time in patients undergoing general anesthesia during surgery with a handheld,

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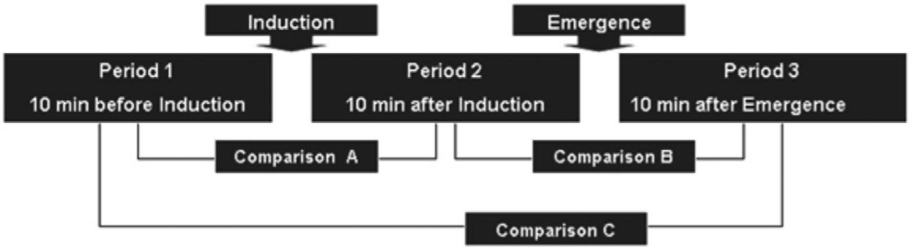

Fig. 1. Three comparisons.

noninvasive device, to characterize the effect of anesthesia. Moreover, we looked at the association between SampEn and different American Society of Anesthesiologists (ASA) classes. We hypothesized that SampEn will decrease after induction of anesthesia but will return to preinduction values after emergence from anesthesia.

2. Methods

After institutional review board approval with waiver of informed consent, patients older than 18 years undergoing elective or urgent abdominal surgery between July 2012 and December 2013 were prospectively enrolled. Patients were enrolled consecutively during daylight hours (convenience sample), when the operating surgeon had no objection to intraoperative heart rate [HR] complexity monitoring. Of note, no surgeon ever objected to research electrocardiogram recording during the study period. Both SampEn and SD of NN intervals ([SDNN], a measure of HRV) were displayed in real time on the monitor; however, only the study staff were privy to the data. The clinical care team was blinded to these data.

Starting 10 minutes before induction of anesthesia, SampEn was recorded with a highly modified [11] ICON Noninvasive Cardiac Monitor (Osypka Medical, La Jolla, CA). The measurements were continued throughout the surgical procedure until 10 minutes after emergence of anesthesia. In addition, continuous measurements of HRV, HR, stroke volume, and cardiac output were also recorded with the same device. Sample entropy was measured through recordings of 200 consecutive beats in a continuous sliding-window fashion [23] as previously described. For the purpose of SampEn calculations, we used a dimension parameter of $m = 2$ and a filter parameter of $r = 20\%$ of the SD. For the HRV measurement, a time-domain analysis of SDNN was calculated [4,10,11].

Additional data collected included age, sex, body mass index (BMI), type of surgery, ASA class, blood pressure (BP), comorbidities (diabetes mellitus, hypertension, ischemic heart disease, etc), β-blocker therapy, the anesthetic medications used during the operation, and hospital length of stay (LOS). Data were entered onto an Excel spreadsheet (Microsoft Excel 2007; Microsoft, Redmond WA).

The primary outcome was the difference in the mean SampEn before, throughout, and after general anesthesia. To investigate the SampEn dynamics, we defined 3 periods, based on 2 key events in anesthesia—induction and emergence. The time before induction of anesthesia was categorized as period 1 (preinduction), the time after induction and before emergence as period 2 (postinduction or intraoperative), and the time after emergence as period 3 (postemergence). We analyzed SampEn changes through these periods and made 3 comparisons: from period 1 with period 2 (comparison A), from period 2 with period 3 (comparison B), and we also compared period 1 with period 3 SampEn (comparison C). Fig. 1 illustrates the different measurement points and comparisons. Secondary outcome was any correlation between the SampEn value in periods 1, 2, and 3 and the different patient characteristics as well as drugs used during anesthesia. The patients fell into 3 ASA classes. We also compared SampEn values between each of the 3 ASA groups for all periods.

Descriptive data are reported as means and SDs, medians, and interquartile ranges or as frequencies (%) as appropriate. Signed rank tests were used to compare the change in SampEn, SDNN, and the vital signs (HR and systolic BP) between the different periods. Wilcoxon rank sum tests were used to compare SampEn or SDNN values between different groups categorized by patient characteristics. Spearman correlation coefficients were used to summarize the relationship between the SampEn/SDNN and other continuous parameters. Multivariable linear regression models including all potential variables significant at 0.10 level in the univariate analysis were used to identify the independent predictors of log-transformed SampEn value at each time point. The SAS version 9.3 (The SAS Institute, Cary, NC) and GraphPad Prism 5.0 (GraphPad Software, San Diego, CA) were used for the statistical analysis. Using a Bonferroni adjustment for 3 comparisons, a 2-sided $P < .017$ was considered statistically significant.

Table 1
Patient characteristics

Characteristic	(n = 128)
Age (y), mean ± SD	50.4 ± 15.5
Male, n (%)	81 (63.3%)
Female, n (%)	47 (36.7%)
Elective surgery, n (%)	94 (73.4%)
Urgent surgery, n (%)	34 (26.6%)
BMI	28.1 ± 5.8
Ischemic heart disease, n (%)	5 (3.9%)
Hypertension, n (%)	45 (35.2%)
Diabetes mellitus, n (%)	12 (9.4%)
β-blockers, n (%)	22 (17.2%)
ASA I, n (%)	28 (21.9%)
ASA II, n (%)	79 (61.7%)
ASA III, n (%)	21 (16.4%)
ASA IV, n (%)	0 (0%)
ASA V, n (%)	0 (0%)
HOS LOS (d), median (interquartiles)	0 (0-3)

HOS, hospital length of stay.

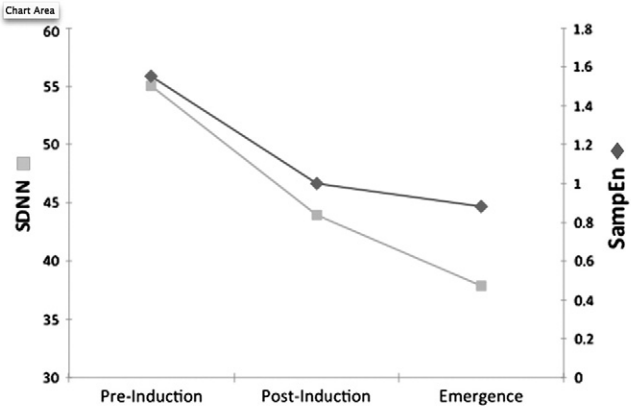

Fig. 2. SDNN and SampEn metrics before induction, after induction, and at emergence.