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Original Research

Heart Rate Variability of Patients with Respect to Induction of Anesthesia in Gynaecologic Surgery: A Cross Sectional Study in Yaounde (Cameroon)

Variabilité de la Fréquence Cardiaque des Patients en Lien avec l'Induction de l'Anesthésie en Chirurgie Gynécologique : Une Étude Transversale dans un Hôpital de Yaoundé (Cameroun)

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ABSTRACT

Introduction. Heart rate variability (HRV) is a well-established quantitative predictor of clinical cardiac events and thus may be an indispensable tool of the anaesthetist, thus motivating our study, with the aim of analysing HRV at induction of anaesthesia. **Materials and Methods.** We carried out a prospective cross-sectional study from the November 1st, 2019 to December 31st, 2021 in the surgical theatres of the Yaounde Gyneco-Obstetric and Pediatric Hospital (YGOPH). All patients presenting for gynaecologic surgery under general anaesthesia, with stable haemodynamic parameters were included. HRV of patients was measured at rest, and in 5-minute segments during induction. Results were analysed with the aid of KUBIOS software. HRV parameters were compared with baseline resting values and presented in tabular form. **Results.** Forty-three patients were included, 25 patients being under the age of 40 years. Induction agents included Propofol, Thiopental and Ketamine in the ratio 38:4: 1. There was a general decrease in HRV of patients, following intravenous induction of aneasthesia. LF/HF (low frequency on high frequency) ratio was significantly increased in the FFT spectrum, suggesting significant sympathetic predorminance over parasympathetic input on the HRV. Advancing age (above 40), obesity, anaemia and hypertension led to decreased HRV with varied contributions of PNS and SNS to individual effects seen. **Conclusion.** HRV in gynaecologic patients decreases with intravenous induction of anaesthesia. Comorbidities further decrease HRV during induction of anaesthesia with various contributions of the sympathetic and parasympathetic system.

RÉSUMÉ

Introduction. La variabilité de la fréquence cardiaque (VFC)est un prédicteur quantitatif bien établi des événements cardiaques cliniques et peut donc être un outil indispensable pour l'anesthésiste. Le But de Notre étude est d'analyser la VFC lors de l'induction de l'anesthésie. **Méthodologie.** Nous avons réalisé une étude transversale prospective du 1er novembre 2019 au 31 décembre 2021 dans les salles d'opération de l'hôpital gynéco-obstétrique et pédiatrique de Yaoundé (YGOPH). Tous les patients se présentant pour une chirurgie gynécologique sous anesthésie générale, avec des paramètres hémodynamiques stables, ont été inclus. La VFC des patients a été mesurée au repos et par segment de 5 minutes pendant l'induction. Les résultats ont été analysés à l'aide du logiciel KUBIOS. Les paramètres de VFC ont été comparés aux valeurs de repos de référence et présentés sous forme de tableau. Résultats: Quarante-trois patients ont été inclus, dont 25 avaient moins de 40 ans. Les agents d'induction comprenaient le propofol, le thiopental et la kétamine dans un rapport de 38:4:1. On a observé une diminution générale de la VFC des patients après l'induction intraveineuse de l'anesthésie. Le ratio LF/HF (basse fréquence sur haute fréquence) a augmenté de manière significative dans le spectre FFT, suggérant une prédominance sympathique significative sur l'entrée parasympathique la VFC. L'âge avancé (plus de 40 ans), l'obésité, l'anémie et l'hypertension ont entraîné une diminution de la VFC .. **Conclusion:** La VFC chez les patients gynécologiques diminue lors de l'induction intraveineuse de l'anesthésie. Les comorbidités diminuent davantage l'HRV lors de l'induction de l'anesthésie, avec diverses contributions du système sympathique et parasympathique.

HIGHLIGHTS OF THE STUDY

What is already known on this topic

Various agents of induction of general anaesthesia have varied effects on heart rate variability (HRV).

What question this study addressed

Heart rate variability of patients with respect to induction of anesthesia in gynaecologic surgery in Yaounde (Cameroon).

What this study adds to our knowledge

1) Induction agents included propofol, thiopental and ketamine in the ratio 38:4: 1.
2) There was a general decrease in HRV of patients, following intravenous induction of aneasthesia.
3) Advancing age (above 40), obesity, anaemia and hypertension led to decreased HRV with varied contributions of PNS and SNS to individual effects seen

How this is relevant to practice, policy or further research.

The anaesthesiologist should be guided on the manipulation of these drugs for induction based on these local data.

INTRODUCTION

Heart rate variability (HRV), is defined as the variation in instantaneous heart rate around its mean[1]. It is a well-established quantitative predictor of clinical cardiac events[2] and may be an indispensable tool of the anaesthetist [1]. As a physiological phenomenon, it goes beyond the heart rate (HR) to reflect the sino atrial nodes (SA node) response to parasympathetic and sympathetic nervous system input. The sympathetic nervous system (SNS) activity increases HR and therefore decreases HRV, whereas the parasympathetic nervous system (PNS) decreases HR and increases HRV [2]. Both play very crucial roles in maintaining homeostasis in response to internal and external stimuli and even during anaesthesia [2, 4]. HRV collection not only provides information of patient's autonomic nervous system status, but appears to provide an accurate assessment of the nociception-analgesia balance in deeply sedated patients and those under general anesthesia and thus may allow tailoring of the analgesia for patients in the operating room [1]. The peri-operative period being a very stresfull period is associated with high morbi-mortality rates especialy in developing nations with an incidence of about 21.97 and 1.12 per 10,000 due to anesthetics [10]. It is known that anaesthetic agents cause an inhibitory effect on the autonomic nervous system tone resulting in hypotension, hypoxia, and cardiac dysrhythmias [11, 12]. Studies of some of theses agents, show a reduction in HRV [11,13, 14]. Whereas, some show that some specific general anesthetic agents have differential effects on the change of HRV when measured after induction of general anesthesia [21]. Most of these studies were carried out under ideal and controlled situations, permiting the study of individual agents used for induction of anaesthesia [15, 16, 17, 18], whereas induction of anaesthesia often involves a combination of several drugs, whose implications are a sum on HRV and are rarely studied. Moreover, in our context, studies on HRV with induction of anaesthesia agents are rare. These aspects motivated our study; a cross-sectional study in a Tertiary center in Yaounde, Cameroon, with the aim of analysing the effects of local intravenous agents of anaesthesia on HRV in women undergoing elective gynaecologic surgery during induction of general anaesthesia (GA). We also aimed to study the impacts of these agents with various patient factors such as age and co-morbidities. Our research questions were: In a population of female patients presenting for gynaecologic surgery, what is the effect of local induction agents for anaesthesia on their heart rate variability? How would patients factors such as age and co-morbidities influence these HRV parameters?

MATERIALS AND METHODS

Design, populations

This was a prospective cross-sectional study that took place from November 1^{st,} 2019 to December 31st, 2020 in the surgical theatres of the Yaounde Gyneco-Obstetric and Pediatric Hospital (YGOPH). Sample size was calculated based on a pre-study estimate of Gynaecologic surgeries of 6,8% in YGOPH. Adult patients programmed for elective gynaecologic surgery under general anaesthesia and who gave informed consent were included in the study. A semi-structured questionnaire was used to collect data from the patients. Instantaneous heart rates of patients were recorded with the aid of a cardio frequency meter, Polar H 10, strapped to the patient's chest via a belt. Recordings were simultaneously transferred via Bluetooth to an android phone and later to a windows 10 computer for analysis. HRV analysis later was with the aid of Kubios version3.1.0 software installed in a windows 10 computer.

Procedures

Anaesthetic files and medical records were exploited, and only patients with normal sinus rhythm on ECG were selected for the study. Other data extracted included, demographic characteristics, weight, height BMI of patients, indication for surgery, past medical, surgical and anaesthesiologic history, Gravidity, toxicology history (tobacco, alcohol), Systemic review parameters (fever, cough, catarrh, bleeding) and ASA status. Heart rate variability variables are represented in the form of time domain, frequency domain and non-linear measurements. Time domain measurements were Root mean square of successive RR interval differences (RMSSD) and MeanRRms. Frequency domain measures were , absolute power of the low-frequency band (LFms2), absolute power of the high-frequency band (HFms2), ratio of LF-to-HF power (LFHF ratio) in both the FFT and AR spectrum. Non- Linear measures are represented by Poincaré plot standard deviation perpendicular the line of identity (SD1) Poincaré plot standard deviation along the line of identity (SD2). The unit of measure of all these parameters being ms.

On the day of surgery, each participant was fitted with a cardiofrequency meter, Polar H10 HR sensor chest strap (see figure.1). The Polar H10 chest strap, detected, collected and processed HRV measurements by detecting the electrical signals of the heart. Instantaneous heart rate was recorded at intervals of 5 minutes; at rest, and during intravenous (IV) induction of anaesthesia. Bluetooth 4.0 signals, transferred the data from the chest device to the Polar beat© app downloaded onto an android phone. Once the device connections were confirmed, recording was commenced by pressing the "start" button on the Polar beat© app. Signal processing later converted the heart's electrical signals (extracted from the ECG QRS complex) into RR intervals with the aid of this app. The raw R-R interval data was then transferred into a windows 10 laptop, and later exported as a text file to Kubios HRV software (version 3.1.0, downloaded onto the Windows 10 laptop) for analysis of HRV parameters within the frequency, time and nonlinear domains.

Fig 1: Patient installation at rest for measurement of HRV, Polar H10 device strapped around chest (Original picture, Nyuydzefon, 2021)

Technique for anaesthesia

All patients included in our study were operated under general anaesthesia with intubation and mechanical ventilation. Prior to induction, patients were pre-oxygenated for 3minutes. Drugs used for induction and the order in which they were administered was as follows, Fentanyl at a dose of 4 µg /Kg followed by the administration of an IV hypnotic agent (propofol at a dose of 3mg/Kg, Ketamine 4mg/Kg or Thiopental 5mg/kg) was used in opioid based anaesthesia for patients. A few patients (five) didn't receive fentanyl, in an opioid free anaesthesia technique. Suxamethonium chloride at a dose of 1mg/kg was used to achieve rapid myorelaxation prior to intubation. After intubation, anaesthesia gases (halothane, Isoflurane and sevoflurane) were used to maintain anaesthesia. The various agents used for induction, grouped according to IV/gaseous hypnotic were as follows **(Table I).**

Table I: The various agents used for induction, grouped according to IV/gaseous hypnotic

Variables	Frequency	(%)
Induction agents used		
halo/ketamine	1	2.3
halo/propofol	25	58.1
halo/thiopental	4	9.3
iso/propofol	10	23.3
sevo/propofol	3	7.0

Halo –Halothane, Iso – Isoflurane, Sevo - sevoflurane

Statistical Analysis

Information extracted was entered in Microsoft Excel Version 10. Data was subsequently exported into STATA 14 for analysis. HRV parameters were determined using the Kubios software program, which analysed the frequency, time and nonlinear parameters of manually corrected R-R data. The data was input into Excel using validity and reliability spread sheets and analysed for all HRV parameters. The autoregressive (AR) algorithm as well as Fast Fournier Transformer (FFT) were used for power spectral analysis of the frequency series and included the log of low frequency (LF), high frequency (HF) and low frequency of high frequency ratio (LF/HF). Time and nonlinear parameters were included for investigation, including mean R-R, standard deviation of normal-to-normal intervals (SDNN), mean square root differences of the standard deviation (RMSSD), HRV triangular index, triangular interpolation of normal-to-normal interval histogram (TINN), standard deviation of instantaneous R-R interval variability (SD1), standard deviation of continuous long-term R-R variability (SD2) and their ratio (SD1/SD2). The difference in mean heart rate variability parameters of participants at rest were compared to the mean heart rate variability during IV induction using the paired student t-test. To assess the effect of confounders, a paired student t-test was used to compare the difference in mean heart variability at rest and the mean heart variability during IV induction after stratification according to the confounder. After the paired student t-test on each variable, the means, difference of mean, 95% confidence intervals and p-values were read-off and recorded. P-values < 0.05 were considered statistically significant.

RESULTS

1. Clinical characteristics of patients

Forty-three female patients were included in our study. Most patients were between the ages of 30 to 40 years old, mean 38.5years. Twenty five patients were less than 40 years and 18 were above the age of 40. The BMI of most patients was normal, 18.5-25(37.2%). Most of the patients 30(69.8%) were classified ASA 2. Hypertension was the most frequent co-morbidity seen in 6 (13.9%) patients. Open laparotomy 22(51.3%) was the most frequent technique used for gynaecologic procedures, while endoscopic gynaecologic surgery was performed in 21 (48.7%) women. Clinical characteristics of patients are represented in table II and III below.

Table II. Distribution of patients by Age and BMI

Variables	Frequency	Percentage (%)
Age (years)		
[20 – 30[	9	20,9
[30 – 40[	16	37,2
[40 – 50[	9	20,9
[50 – 60[	7	16,3
≥ 60	2	4,7
BMI (kg/m²)		
[18,5 – 25[	16	37,2
[25 – 30[	12	27,9
[30 – 35[	7	16,3
[35 – 40[	5	11,6
≥ 40	3	7

Table III. ASA classification and Co-morbidities of patients

Variables	Number	(%)
ASA Class		
ASA 1	4	9,3
ASA 2	30	69,8
ASA 3	9	20,9
Past Medical History		
Diabetes	1	2,3
Hypertension	6	13,9
Asthma	2	4,7
HIV	4	9,3
Hepatitis B	1	2,3
Gastritis	2	4,7
Gout	1	2,3
Toxicology		
Alcohol	18	41,9
Tabacco	1	2,3

Changes in heart rate variability of patients during induction following intravenous administration of Anaesthesia:

Heart rate variability at rest compared with that during intravenous induction of anaesthesia revealed a non statistically significant increase in HRV in the LF spectrum as well as in the HF spectrum. Similar results were seen in non-linearity parameters , SD 1 and SD2. However, LF/HF ratio was significantly increased in the FFT spectrum, suggesting sympathetic dominance. **Table IV** shows HRV during intravenous induction of anaesthesia when compared with values at rest.

Table IV: Comparison of HRV parameters during IV induction of anaesthesia versus during rest

HRV Parameter	Induction	Rest	difference	95% CI	P
LFms2FFT spectrum	92.8	61.9	30.9	-5.62701 67.40727	0.095
LFms2AR spectrumB	27850.8	109.3	27741	-25527.5 – 81010.5	0.299
HFms2FFT spectrum	13.2	11.3	1.9	-6.2 – 10.0	0.638
HFms2AR spectrum	15.7	11.4	4.4	-6.5 – 15.3	0.424
LFHFratio FFTspectrum	19.0	7.6	11.4	3.0 – 19.7	0.009*
LFHFratio AR spectrum	885.4	15.7	869.6	-873 - 2612	0.320
SD1ms	4.5	3.9	0.6	-0.1 – 2.1	0.466
SD2ms	22.3	13.2	9.1	4.6 – 22.7	0.188
RMSSDms	6.2	5.5	0.7	-1.4 – 2.9	0.487
MeanRRms	708.4	730.5	-22.7	72.0– 27.7	0.375

Analysis of the influence of age and comorbities on HRV at Induction

1. Effect of Age on HRV at induction

During IV induction, there was a significant dominance of sympathetic over parasympathetic influence on HRV in patients under 40years of age . However, in those over 40years of age this wasn't seen . Table V below shows HRV parameters with respect to patients' age groups, less than 40 and above 40 years.

2. Effect of BMI on HRV at IV Induction

During IV induction, a significant decrease was seen in HRV in obese patients as seen in significantly decreased mean RRms values. However, no significant drop in HRV was seen in non-obese subjects. However, it was not possible statistically to show any implications of either the parasympathetic or sympathetic system in these observations. Table VI below shows the different HRV in patient groups, obese vs non-obese.

3. Effect of Anaemia on HRV during IV Induction

Intravenous induction of anaesthesia was shown to cause a predominance of sympathetic (over parasympathetic) tone on HRV, (LF/HF spectrum) in anaemic patients. No significant influence was seen in non-anaemic patients. Table VII below shows HRV changes during IV induction of anaesthesia in anaemic and non-anaemic subjects.

4. Effect of Hypertension on HRV at IV Induction

Patients with hypertension demonstrated a 10-fold decrease in HRV as compared to patients without HBP at induction of anaesthesia with IV agents. Table VIII below shows the changes in HRV parameters for either hypertensive and non-hypertensive patient groups during IV induction of anaesthesia.

5. Effect of ASA status on HRV at IV Induction

ASA 1 and 2 patients demonstrated increased sympathetic predominance under IV induction of anaesthesia as compared to ASA 3and 4 patients who experienced no significant change in HRV parameters following IV induction of anaesthesia. Table IX below shows HRV of ASA 1&2 alongside those of ASA 3&4 patients during IV induction of anaesthesia.

Table V: HRV during IV induction in patients less than 40 years and in those greater than 40 years

HRV Parameter	< 40 Years					>= 40 Years				
	IV Induction	Rest	difference	95% CI	P	IV Induction	Rest	difference	95% CI	P
LFms2FFTspectrum	103.9	74.5	29.4	21.5 – 80.3	0.245	77.5	44.5	33.0	-24.3 – 90.2	0.241
LFms2ARspectrum	2452.6	73.7	2378.9	2453.2- 7211	0.320	63126.0	158.7	62967.3	-700065.6 - 196000.2	0.332
HFms2FFTspectrum	13.3	14.4	1.1	14.2–12.0	0.865	12.9	6.9	6.1	1.9 - 14.0	0.125
HFms2ARspectrum	19.0	14.5	4.5	-14.0 – 23.1	0.617	11.2	7.1	4.1	-3.8 – 12.0	0.289
LFHFratioFFTspectrum	20.9	7.4	13.4	0.8 – 26.1	0.038	19.4	7.9	8.5	-2.3 – 19.2	0.114
LFHFratioARspectrum	26.1	6.6	19.5	-4.1 – 43.1	0.101	2078.7	28.3	2050.4	-2304.0 – 6404.9	0.334
SD1ms	4.9	4.2	0.7	-2.0 – 3.3	0.610	3.9	3.5	0.4	-0.6 – 1.4	0.376
SD2ms	27.0	14.6	12.4	-11.5 – 36.3	0.296	15.8	11.3	4.9	-0.7 – 9.7	0.085
RMSSDms	6.9	5.9	0.9	-2.8 – 4.6	0.620	5.4	4.8	0.5	-0.8 – 1.9	0.411
MeanRRms	7.2.1	703.6	-1.5	-74.5 – 71.6	0.927	717.0	767.9	-50.9	-119.7 – 17.0	0.138

Table VI: Changes in HRV in obese and non-obese subjects during IV induction of Anaesthesia

HRV Parameter	BMI<30					BMI>=30				
	IV Induction	Rest	Difference	95% CI	P Value	IV Induction	Rest	Difference	95% CI	P Value
LFms2FFTspectrum	90.3	67.8	22.6	-22.5 – 67.6	0.312	97.4	511	46.4	-23.2 – 116.0	0.175
LFms2ARspectrum	2183.3	68.3	2115.0	-2175.2 – 6405.1	0.320	75763.4	185.7	75577.7	-86708.0 – 237863.4	0.335
HFms2FFTspectrum	16.3	11.8	4.5	-7.5 – 16.5	0.450	7.3	10.2	-2.9	-10.5 – 4.7	0.421
HFms2ARspectrum	18.6	11.5	7.1	-9.3 – 23.5	0.383	10.5	11.2	-0.7	-10.0 – 8.6	0.870
LFHFratioFFTspectrum	16.3	8.1	8.2	-1.0 – 17.5	0.078	24.0	6.8	17.2	-0.7 – 35.1	0.059
LFHFratioARspectrum	25.2	7.4	17.8	-3.3 – 38.8	0.095	2491.0	31.2	2459.9	-2862.6 – 7772.3	0.337
SD1ms	4.9	4.0	1.0	-1.4 – 3.3	0.403	3.7	3.8	-0.7	-1.5 – 1.1	0.776
SD2ms	26.4	13.8	12.6	-8.6 – 33.8	0.233	14.6	12.1	2.4	-3.1 – 8.0	0.357
RMSSDms	6.9	5.6	1.3	-1.9 – 4.6	0.415	5.1	5.4	-0.3	-2.1 – 1.5	0.734
MeanRRms	729.9	709.4	20.5	-457 – 86.8	0.530	668.2	770.0	-101.8	-162.6 – 41.0	**0.003**

Table VII: HRV changes during IV induction of anaesthesia in anaemic and non-anaemic subjects.

HRV Parameter	Haemoglobin <13					Haemoglobin>=13				
	IV Induction	Rest	difference	95% CI	P Value	IV Induction	Rest	difference	95% CI	P Value
LFms2FFTspectrum	96.0	70.1	25.9	-14.6 – 66.3	0.202	82.4	35.0	47.5	-51.0 – 145.9	0.303
LFms2ARspectrum	1882.4	69.8	1812.6	-1800.3 – 5426.5	0.314	113546.6	239.8	1133.6.9	-143468.8 – 370082.6	0.344
HFms2FFTspectrum	15.4	12.7	2.7	-7.9 – 13.3	0.607	5.7	6.5	-0.7	-5.6 – 4.1	0.736
HFms2ARspectrum	18.4	12.0	6.4	-7.7 – 20.5	0.364	7.0	9.3	-2.3	-11.0 – 6.3	0.555
LFHFratioFFTspectrum	19.8	7.8	12.0	1.4 – 22.6	0.027	16.2	7.0	9.2	-1.8 – 20.2	0.092
LFHFratioARspectrum	23.8	7.4	16.4	-1.7 – 34.4	0.074	3728.5	43.0	3685.5	-4722 – 12093.5	0.347
SD1ms	4.8	3.9	0.9	-1.1 – 2.9	0.370	3.4	3.9	-0.5	-2.2 – 1.2	0.537
SD2ms	24.8	13.3	11.5	-6.4 – 29.3	0.200	14.0	12.9	1.1	-7.6 – 9.9	0.770
RMSSDms	6.7	5.5	1.2	-1.6 – 4.0	0.387	4.8	5.5	-0.7	-3.1 – 1.7	0.536
MeanRRms	707.8	710.1	-2.3	-59.5 – 54.8	0.935	710.1	797.7	-87.6	-198.4 – 23.3	0.108

Table VIII: HRV changes during IV induction in hypertensive and in non-hypertensive patients

HRV Parameter	Hypertensive					Non-Hypertensive				
	IV Induction	Rest	difference	95% CI	P Value	IV Induction	Rest	difference	95% CI	P Value
LFms2FFTspectrum	114.4	39.1	75.3	20.9 – 129.8	0.016	89.3	65.6	23.7	-18.0 – 65.4	0.257
LFms2ARspectrum	124.9	350.8	-225.9	-1026.5 – 574.7	0.501	32346.9	70.1	-32276.7	-29922.7 – 94476.2	0.300
HFms2FFTspectrum	4.1	10.2	-6.1	-23.4 – 11.3	0.408	14.6	11.4	3.2	-6.0 – 12.4	0.484
HFms2ARspectrum	4.9	9.7	-4.8	-17.1 – 7.5	0.365	17.5	11.7	5.8	-6.8 – 18.5	0.353
LFHFratioFFTspectrum	44.7	7.8	36.9	-1.8 – 75.7	0.057	14.8	7.6	7.2	-0.5 – 15.0	0.066
LFHFratioARspectrum	29.3	63.1	-33.8	-171.6 – 103.9	0.556	1024.2	8.0	1016.2	-1018.7 – 3051.1	0.318
SD1ms	3.3	3.6	-0.3	-1.8 – 1.2	0.641	4.7	4.0	0.7	-1.1 – 2.5	0.432
SD2ms	18.1	12.1	6.0	-1.5 – 13.6	0.095	22.9	13.4	9.6	-6.4 – 25.5	0.233
RMSSDms	4.7	5.1	-0.4	-2.5 – 1.8	0.663	6.5	5.6	0.9	-1.6 – 3.4	0.454
MeanRRms	668.4	766.4	-98.0	-281.7 – 85.7	0.229	714.8	724.7	-9.8	-62.8 – 43.2	0.709

Table IX: HRV changes during IV induction in ASA 1and 2 subjections and in ASA 3 and 4 subject groups.

HRV Parameter	ASA 1 & 2					ASA 3 & 4				
	IV Induction	**Rest**	**difference**	**95% CI**	**P Value**	**IV Induction**	**Rest**	**difference**	**95% CI**	**P Value**
LFms2FFTspectrum	95.8	64.9	30.9	-13.8 – 75.6	0.169	81.5	50.6	30.9	-30.0 – 91.7	0.276
LFms2ARspectrum	33463.8	68.4	33395.4	-34513.8 – 101304.7	0.324	6646.0	263.9	6382.1	-8668.2 – 21432.7	0.357
HFms2FFTspectrum	14.9	12.0	2.9	-7.0 – 12.9	0.557	6.6	8.5	-1.9	-13.7 – 9.9	0.718
HFms2ARspectrum	11.6	12.2	-0.6	-7.0 – 5.8	0.852	31.3	8.2	23.1	-29.6 – 75.8	0.341
LFHFratioFFTspectrum	17.0	7.3	9.7	0.9 – 18.5	0.031	26.5	8.9	17.7	-8.5 – 43.8	0.158
LFHFratioARspectrum	1105.5	7.3	1098.2	1123.6–3320.	0.322	53.6	47.2	6.4	106.5–19.4	0.899
SD1ms	3.9	4.2	-0.3	-1.0 – 0.4	0.423	6.8	3.0	3.8	-4.1 – 11.6	0.301
SD2ms	15.6	13.8	1.8	-1.5 – 5.1	0.285	47.5	10.8	36.6	36.0 – 109.3	0.278
RMSSDms	5.4	5.8	-0.42	-1.4 – 0.5	0.371	9.4	4.2	5.2	-5.7 – 16.1	0.304
MeanRRms	723.6	740.3	-16.7	-72.5 – 39.0	0.546	650.9	693.6	-42.6	180.2 – 95.0	0.496

DISCUSSION

The aim of our study was to evaluate heart rate variability for various patients during induction of general anaesthesia for gynaecologic surgery. We recruited 43 female patients, presenting for gynaecologic surgery who fitted our criteria. HRV of patients was recoreded at rest, and through out induction of general anaesthesia, with the aide of Polar H10 cardiogfrequency meter, and interpreted via the Kubios software. Patients in our study were of the female sex, majority being under the age of 40 years, 25 (58.14%). In this group, 16(64%), were in the age range of 30-40 years. This corresponds to the age range at which most gynaecological surgeries take place[17], [18]. Obese patients constituted 34.9 %, (n=15), among whom, morbidly obese patients, constituted 20% (n=3) of the population however , most patients were mostly non-obese, 28 (65.1%) patients.. Similar rates were found among women in a Jordanian study,[19], as well as in Bangladesh among women of reproductive age [20]. Obesity is global health problem, thus warranting, its consideration in our study of patients HRV. Another major comorbidity noticed amongst our patients was pre-operative anaemia. Most of the patients were anaemic with mean Haemoglobin (Hb) being 11.8g/dl±1,7. Anaemia has been shown to negatively affect cardiovascular activity and this could in turn have an influence on the autonomic activity as well [21] [22]. We thus attempted to explore its impact on HRV during induction of anaesthesia. Other comorbidities seen in patients in our study were hypertension 6(13.9%), asthma, 2 (4.7%) and diabetes, 1(2.3%) and we used ASA status to look at patient's overall fitness. There was a general decrease in HRV of patients, following intravenous induction of aneasthesia. Non-linear spectroscopic measures revealed significant sympathetic predorminance over parasympathetic input on the HRV, likely explaining the decreased HRV. Most of our patients were induced with Propofol, followed by thiopental and ketamine in the ratio 38:4:1. In a bid to understand what exactly happens in the ANS and CNS during induction, Sattine et al, studied the effects of Propofol at induction in both the CNS and ANS and found that HRV analysis was associated with a progressive decrease in complexity and a consequent increase in the regularity indexes. They found that anaesthesia with propofol led to bradycardia which was accompanied by an increase in cardiac sympathetic modulation and a decrease in cardiac parasympathetic modulation during the induction [23].This is very similar to the finding in our study, as we illustrated sympathetic predorminace at induction, with overall decrease in HRV. Similarly, a study by Singh and P.K to quantify autonomic activity during anaesthesia with ketamine revealed that it led to decrease in HRV, but with a sympathetic predorminance over the parasympathetic influence[24]. Increase in sympathetic over parasympathetic dominance with these agents could explain the reason for respiratory depression, when these agents are used in anaesthesia. In a study on the differential effects of thiopental and propofol on HRV during fentanyl based induction of general anaesthesia, both agents were shown to decrease HRV and decreased HF power. Thiopental increased LF power and LF/HF ratio, indicating that its vagolytic effect is associated with increase in sympathetic activity[25]. Propofol however preserved the LF power in this study, indicating that the cardiac parasympathetic activity is reduced more than the sympathetic activity[25]. All the above studies of the various agents, Propofol, Thiopental and Ketamine are in line with our findings, which revealed decreased HRV during induction with these agents, and generally sympathetic predominance. In healthy subjects, HRV is shown to decrease with increasing age, with age having a greater impact than sex on HRV[26] [27]. This doesn't seem to change, and if anything may only worsen when patients with advancing age are subjected to general anaesthesia, due to the inhibitory effect of anaesthesia on HRV. Our study reveals that, though HRV decreased under IV induction in both age groups, patients above 40 experienced more profound decrease in HRV following induction of anaesthesia. A sympathetic predominance was seen in patients below 40 years old during IV induction. This effect was absent for those above 40 years, during IV induction as well as during introduction of gases for all the age groups. Studies show a decrease in HRV with advancing age during induction, just as was the case in our study[28] [29]. Obesity, defined as BMI > 30kg/m2 has been shown to be associated with a higher prevalence of cardiovascular disease[30] [31]. It is supposed that, this could be due to autonomic dysfunction and/or metabolic disorder[30] [32] . The alterations in cardiac autonomic functions thus bring out the changes in the heart rate variability (HRV) indicators[5] [33]. Studies of HRV on obese subjects tend to show decreased HRV when compared to healthy subjects. This particularly being due to decreased parasympathetic tone[34] [35]. In our study, IV induction, led to a significant decrease in HRV in obese patients as seen in significantly decreased mean RRms values. No significant drop in HRV was seen in non-obese subjects. However, it was not possible statistically to show any implications of either the parasympathetic or sympathetic system in the former group. When considering anaemic patients, , intravenous induction of anaesthesia was shown to cause a predominance of sympathetic over parasympathetic tone on HRV, (LF/HF spectrum) during induction in anaemic patients. No significant influence was seen in non-anaemic patients. Yokusoglu et al,2007 found that, iron deficiency anaemia in patients not subject to anaesthesia, was associated with lower HRV values when compared subjects in the control group, reflecting parasympathetic withdrawal[36]. They speculated a probable link between anaemia and the accentuated sympathetic activity that may be triggered by hypoxia sensed through carotid bodies[36]. In both ASA 1&2 and ASA3&4 patient groups, a decrease in HRV was seen. However, ASA 1 and 2 patients demonstrated significant increased sympathetic predominant activity, as compared to resting values following IV induction. Patients with hypertension demonstrated a 10-fold decrease in HRV as compared to patients without HBP at induction of anaesthesia with IV agents. HRV is seen to be reduced in men and women with systemic hypertension[37] [38]. In anaesthesia, diabetes, hypertension are both factors that are associated with low HRV and could be prognostic on per-operative cardiac events[35] [30]. In our study, Patients with hypertension demonstrated a 10-fold decrease in HRV as compared to patients without HBP at induction of anaesthesia with IV agents.

Limitations

Our study was carried out in a single center, this together with our sample size could limit the generalizability of our study out of YGOPH. Male patients were not also studied, which could limit the generalizability of our results to this sex. We had no influence on the technique of anaesthesia, as a result, our patients were subject to different drug combinations, making us have several little groups, and also patients subjected to different drugs such as in premedication, whose effects on HRV in combination with the drugs used in anaesthesia may have influenced our results. Finally, the COVID 19 pandemic which was at its peak during the recruitment period, limited study population, as many staff were affected. Patients had to put on face masks, which is a factor not studied in many studies with which we compared our study.

Conclusion

At the end of our study, we conclude that there was a general decrease in HRV of patients, following intravenous induction of aneasthesia, with significant sympathetic predorminance over parasympathetic input on the HRV. This could be transcribed to the effect of propofol in most of these cases as it was the main IV agent used. Advancing age (above 40), obesity, anaemia and hypertension led to decreased HRV with varied contributions of PNS and SNS to individual effects seen.

Conflict of Interest

The authors declare no conflict of interest.

Contributions of authors

Berinyuy: Design of study and writing of paper. **Azabji:** study design and editing of article. **Djientcheu:** statistical analysis and editing. **Brian Ajong** Statistical analysis and editing**. Ze Minkande :** Design and editing

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