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Heart Rate Variability analysis for arterial hypertension etiological diagnosis during surgical procedures under tourniquet.

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Abstract—**Pneumatic tourniquets are widely used to provide a bloodless operative field during upper or lower limb surgery. If tourniquet inflation during general anesthesia is initially a mild stimulus, a long duration of inflation can imply heart rate and blood pressure increasing. However, heart rate or blood pressure increasing can also be caused by other external stimuli. Indeed, in the case of an insufficient analgesia, painful surgical stimuli can also cause an increase in heart rate and blood pressure. Therefore, in the case of the use of a tourniquet during surgery, it's very difficult for the anesthesiologist to distinguish hypertension caused by pain from hypertension caused by tourniquet inflation. In such a case, an efficient and reliable hypertension diagnosis could help the anesthesiologist in the medication choice. We have previously developed and evaluated an Analgesia / Nociception Index (ANI) based on the magnitude analysis of the respiratory patterns on the RR series. We hypothesize that the use of such an index could help in the arterial hypertension etiological diagnosis during surgical procedures under tourniquet.**

Keywords—**Analgesia/Nociception Index, Arterial Hypertension, Tourniquet**

I. INTRODUCTION

PNEUMATIC tourniquets are widely used during orthopedic surgical procedures [1]. Such devices prevent blood flow to a limb and enable surgeons to work in a bloodless operative field. This allows surgical procedures to be performed with improved precision, safety and speed.

If tourniquet inflation during general anesthesia (GA) is initially a mild stimulus, a long duration of inflation can implies heart rate (HR) and arterial blood pressure (ABP) augmentation. In that case, the deepening of GA can't block the hemodynamic reaction and the injection of an antihypertensive agent (like nicardipine, Loxen®) is needed to decrease ABP. However, ABP increasing can also be caused by other external stimuli. Indeed, in the case of an insufficient analgesia, painful surgical stimuli can also cause an arterial hypertension (AHT) episode. In that case, a bolus of opioid (like Sufentanil) is needed to decrease ABP.

In the particular case of the use of a tourniquet during surgery, it's very difficult for the anesthesiologist to distinguish AHT episode caused by pain from AHT episode cause by tourniquet long-term inflation. Therefore, an efficient and reliable pain measurement system could help in AHT diagnosis and then allows to guide the anesthesiologist in the medication choice. In that way, such a system would reduce the AHT duration and would avoid useless opioid injections.

Several studies have shown that Heart Rate Variability (HRV) analysis gives information related to the Autonomic Nervous System (ANS) activity [2, 3]. The strong influence of anesthetic drugs over the ANS lead some authors to test whether HRV could be used as an anesthesia global depth measure [4, 5], but no one described a measure specific of the pain / analgesia balance during GA.

HRV is mediated primarily by changing levels of parasympathetic and sympathetic outflow from the central nervous system to the sinoatrial node of the heart. Studies using selective pharmacological blockade of the cardiac sympathetic and parasympathetic receptors have shown that fluctuations in HRV above 0.15 Hz are mediated exclusively by changes in parasympathetic outflow; on the other hand, low frequency changes are mediated by both parasympathetic and sympathetic activities [2]. In adults, growing evidence highlights that pain results in a decrease of HRV, in particular of the high frequency (HF) power (0.15 - 0.4 Hz), indicating a drop of vagal tone during unpleasant stimuli or emotions [6,7,8]. During surgical procedure in adult patients, HRV is correlated with the balance between the nociceptive stimulus and the level of analgesia [9].

We have previously described and evaluated a pain / analgesia balance measurement algorithm using HRV analysis [9, 10]. In this paper, we hypothesize that the use of such an index could help in the AHT etiological diagnosis during surgical procedures under tourniquet.

II. METHODS AND MATERIALS

Our method to evaluate pain is based on a time analysis of HRV. Recording RR series during general anesthesia allowed us to observe the change of patterns in relation to surgical stimulation. We noted that, when anesthesia is well stabilized, the RR series is only modulated by Respiratory Sinus Arrhythmia (RSA), so that a ventilatory pattern appears at regular intervals on the RR series (figure 1a). These patterns become irregular or chaotic (figure 1b) as soon as anesthesia is disturbed by any external event. Especially, we found that painful events, such as surgical incision, induced a decrease of the patterns magnitude.

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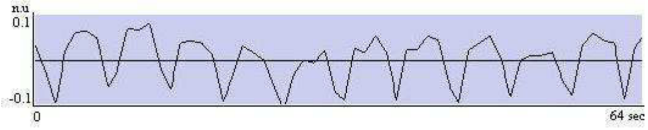

Fig. 1a: RR series in case of well-stabilized anesthesia.

Fig. 1b: RR series in case of painful event.

According to these observations, we developed a pain level evaluation algorithm based on the magnitude analysis of the respiratory patterns on the RR series [11], as described below.

A - ANI computation:

The 250 Hz digitized electrocardiogram (ECG) is used to automatically detect R waves [10], and thus measure heart periods, which is the time between RR intervals. RR intervals series are filtered in real time using an effective filtering algorithm preventing from artefacts-induced inaccurate measurement of RR intervals series [12].

To obtain parameters values free of inter patient's variability, the signal is normalized within the moving window. In a first step, the normalization algorithm consists of computing the mean (M) value.

$$M = \frac{1}{N}\sum_{i=1}^{N}(RR_i)$$

Where RR_i represents the RR samples values and N the number of samples in the window. Then the mean value M is subtracted from each sample of the window.

$$RR_i = (RR_i - M).$$

The resulting RR series is then used for the norm (S) value computation.

$$S = \sqrt{\sum_{i=1}^{N}(RR_i)^2}$$

Finally, each resulting RR sample is divided by the norm value S.

$$RR_i = RR_i / S$$

Since the method is based on the magnitude analysis of the respiratory patterns on the RR series, RR samples are high pass filtered between 0.15 and 0.5 Hz (corresponding to the parasympathetic HR activity) using a wavelet based numerical filter. Computing the area under the RR series curve values as shown in figure 2 assesses the parasympathetic tone activity. Local minima and maxima are detected, and the areas A1, A2, A3 and A4 are measured as the area between the lower and upper envelopes in each 16 sec sub-window.

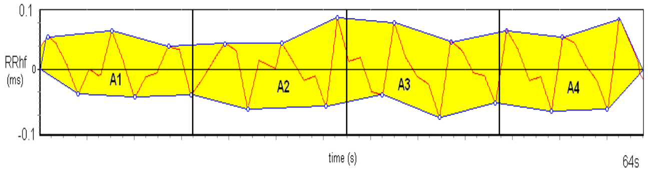

Fig. 2 Local minima and maxima detection and A1, A2, A3, A4 computation.

We defined AUCmin = min(A1,A2,A3,A4). ANI is then computed in order to express a fraction of the total window surface, leading to a measure between 0 and 100:

$$ANI = 100 * [\alpha * AUCmin + \beta] / 12.8$$

Where $\alpha = 5.1$ and $\beta = 1.2$ have been determined in order to keep the coherence between the visual effect of respiratory influence on RR series and the quantitative measurement of ANI [9].

B – Clinical trial

To test the ability of our HRV analysis method for AHT etiological diagnosis, we recorded RR series on patients planned to undergo GA for total knee replacement under tourniquet. Anesthetic protocol comprised propofol (hypnotic drug) delivered by a target-controlled device (Orchestra® Base Primea, Fresenius Kabi, France) and Sufentanil (opioid) delivered by bolus. Propofol target was adapted in order to maintain the bispectral index (BIS®, Aspect Medical System) in the predefined range of [20-50]. The surgical and anesthetic procedures were not altered by inclusion in the study; in the case of an increase of more than 20% of the ABP (AHT episode), one or several Sufentanil bolus were delivered. If ABP didn't decrease significantly during the next 10 minutes, a bolus of Loxen® was delivered. Medical staff was blind to the ANI monitor, in order not to affect their decisions for anesthetic and surgical management.

We decided to report all AHT episodes and to divide the whole population in two groups; group 1) *Low ANI* (ANI<60%) and group 2) *High ANI* (ANI >60%). A Student t test was used to compare the different instants; During the AHT (*AHT*), after Sufentanil injections (*Aft-Suf*) and after Loxen® injection (*Aft-Lox*). p<0.05 was considered as significant.

III. RESULTS

17 patients have been included in this prospective observational study. The 17 resulting records were from 110 minutes to 146 minutes durations. In this population, we reported 8 AHT episodes with *Low ANI* (Group 1) and 11 AHT episodes with *High ANI* (Group 2).

In the group 1, ABP was significantly lower after the Sufenta injections (p<0.05); none Loxen® injection has been needed. ANI was significantly higher after Sufenta injection ($p<0.01$).

Table 1: parameters values for group 1. Values are median (25–75% interquartile range). Statistical analysis = Student t test.

	AHT	Aft-Suf	p
ANI (%)	43 [37-55]	77 [68-90]	0.018
ABP (mmHg)	148 [132-150]	117 [102-124]	0.018

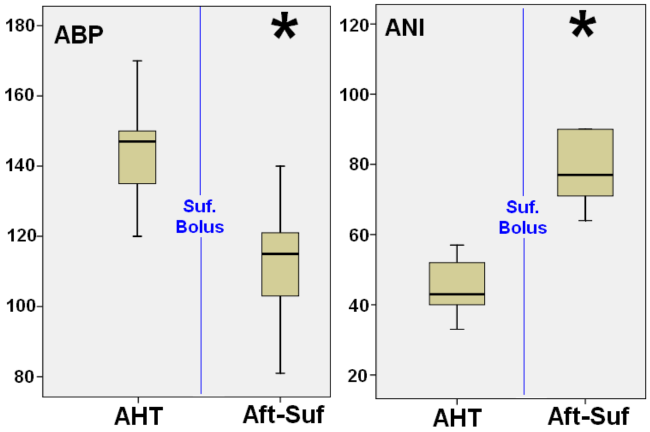

Fig. 3 : AHT = Group 1 ABP and ANI values during AHT **;**
Aft-Suf. = Group1 ABP and ANI values after Sufentanil bolus.
Statistical analysis = Student t test. * **p<0,01 vs AHT.**

In the Group 2, all the Sufentanil injections have been useless to reduce ABP. For these 11 cases, a Loxen® injection has been necessary. In each case, ABP was significantly lower after the Loxen® injection ($p<0.01$). There were no significant differences in ANI between *AHT*, *Aft-Suf* and *Aft-Lox*.

Table 2: parameters values for group 2. Values are median (25–75% interquartile range). Statistical analysis = Friedman non parametric statistical test.

	AHT	Aft-Suf	Aft Lox	p
ANI (%)	77 [64-90]	81 [70-95]	74 [59-84]	NS
ABP (mmHg)	160 [150-171]	160 [155-171]	120 [109-125]	<0.01

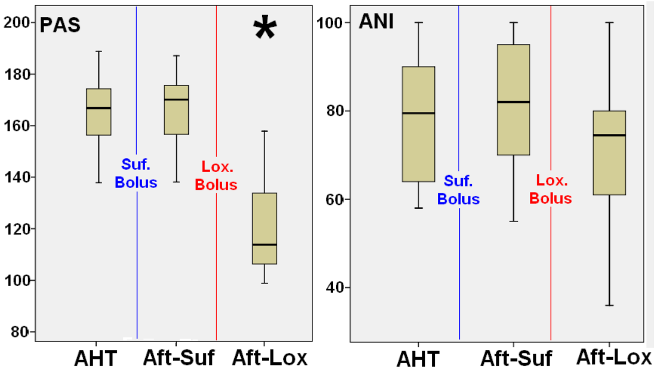

Fig. 4 : AHT = Group 2 ABP and ANI values during AHT **;**
Aft-Suf. = Group 2 ABP and ANI values after Sufentanil bolus **;**
Aft-Lox = Group 2 ABP and ANI values after Loxen bolus.
Statistical analysis = Student t test. * **p<0,01 vs AHT.**

In the two groups, no specific HR variation has been observed between the *AHT* and the *Aft-Suf* instants. For the group 2, a short HR increasing has been observed after Loxen® injection.

IV. CONCLUSION

In this paper, we hypothesized that the use the analgesia nociception index (ANI) could help in the AHT etiological diagnosis during surgical procedures under tourniquet. Indeed, in the particular case of the use of a tourniquet during surgery, it's very difficult for the anesthesiologist to distinguish AHT episode caused by pain from AHT episode cause by long-term tourniquet inflation implying some difficulties in the medication choice.

This preliminary study shows that in the case of a low ANI (<60%) a Sufentanil injection is efficient to reduce ABP. In such a case, we can observe that ABP is significantly lower after Sufentanil injection while ANI is significantly higher; we can conclude that AHT was the result of a painful stimulus perception due to insufficient analgesia.

On the other hand, in the case of a high ANI (>60%), Sufentanil injections are not efficient for AHT suppression. We observe no significant changes in ABP and ANI, which could be interpreted as a painless AHT episode. In such a case, a Loxen® injection is efficient to suppress AHT. ABP is significantly reduced while we observe no significant changes in ANI.

This study shows the ability of the ANI for the etiological diagnosis of AHT during surgical procedures under tourniquet. The use of ANI during such surgical procedures could drive the anesthesiologist and therefore reduce his decision time and avoid useless opioids injections.

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