Arterial blood pressure regulation following aorta clamping and declamping during surgery

Manuela Ferrario, *Member, IEEE*, Federico Aletti, *Member, IEEE*, Nicola Toschi, Antonio Canichella, Filadelfo Coniglione, Elisabetta Sabato, Florencia della Badia Giussi, Mario Dauri, Alessandro F. Sabato, Maria Guerrisi, Sergio Cerutti, *Fellow, IEEE*

Abstract—In this paper, we propose the use of black box models for the system identification of the cardiopulmonary baroreflex control of arterial resistance and of ventricular contractility and of arterial baroreflex control of heart rate (HR) from invasive, continuous measurements of arterial blood pressure (ABP) and central venous pressure (CVP), and non invasive, continuous recordings of ECG and respiration. Two crucial phases of the abdominal aortic aneurism (AAA) repair were investigated: the clamping and declamping of aorta. The objective of the present work is to evaluate and to test the ability to monitor baroreflex responses to clamping and declamping maneuvers preceding and following aneurism removal.

I. INTRODUCTION

T HE analysis and modeling of short term cardiovascular (CV) variability can provide with a powerful insight the autonomic nervous system control of circulation [1,2]. Securing hemodynamic stability in order to prevent hypotension and organ perfusion deficiencies is one of the main challenges faced by the anesthesiologist or intensivist during major surgery as well as in the intensive care unit. In this context, one of the most commonly practiced maneuvers is intravenous administration of colloids or crystalloids, where increasing circulating volume will aid in maintaining arterial blood pressure (ABP) through modulation of arterial resistances and ventricular contractility mediated by the cardiopulmonary baroreflex.

In this paper, we propose the use of black box models for the system identification of the cardiopulmonary baroreflex control of arterial resistance and of ventricular contractility and of arterial baroreflex control of heart rate (HR) from invasive, continuous measurements of ABP and central venous pressure (CVP), and non invasive, continuous recordings of ECG and respiration [3]. These models were applied to the analysis of a standard surgical procedure. CV signals were continuously recorded during open surgical

This work was supported by Italian Ministry of Education, University and Research (MIUR), FIRB2008, Project RBFR08VABD.

F. Coniglione, E. Sabato, F. della Badia Giussi, M. Dauri, A.F. Sabato are with Department of Anesthesia and Intensive Care Medicine, University of Rome "Tor Vergata", Roma, Italy.

N. Toschi, A. Canichella, M Guerrisi are with the Medical Physics Section, University of Rome "Tor Vergata", Via Montpellier 1, 00133 Roma, Italy. repair of abdominal aortic aneurism (AAA).

In particular, two crucial phases of the intervention were investigated: the clamping and declamping of aorta, which precede and follow the surgical removal of the aneurism. Typical maneuvers consist in the infusion of vasodilators just before the clamping, and in the infusion of vasoconstrictors and/or fluids during the declamping of the aorta. These phases are very challenging as changes in total peripheral resistance and hemodynamics are sudden and marked.

The choice of this type of procedure is motivated by the fact that it is quite standard and the timing of the events well established. The objective of the present work is to evaluate and to test the ability to monitor the baroreflex responses to clamping and declamping maneuvers preceding and following aneurism removal.

II. METHODS

A. Data collection

A custom software was developed (termed "Global Collect", Labview 2009© environment) in order to simultaneously acquire, interpret and visualize data from multiple patient monitors, including the GE S/5 Avance Carestation©, Pulsion PiCCO©, Edwards Vigileo©. All devices perform internal A/D conversion and transmit data (RS232 interfaces) sampled at heterogeneous frequencies and packaged through proprietary protocols. Custom interpreter modules were built based on protocol information obtained from device manufacturers and integrated into a single application which provides the user with flexible synchronised waveform and indices acquisition as well as on-screen visualization through a multiple RS232-USB 2.0 Hub.

Four surgical interventions were analyzed. Patients underwent the same procedures: open AAA surgery, sedation induced by a bolus of propofol (2mg/kg) and sedation maintenance by a total intravenous anesthesia (TIVA, 6-8 mg/kg·hr).

B. Pre-processing of signals

Pre-processing of raw recordings of ABP, CVP, ECG and respiration (Airway Pressure, Airway Flow, CO_2 and O_2 relative concentrations) was performed in order to extract beat-by-beat series, employing standard and robust

M. Ferrario, F. Aletti and S. Cerutti are with Dipartimento di Bioingegneria, Politecnico di Milano, Piazza Leonardo da Vinci 32, 20133 Milano, Italy (e-mail: <u>manuela ferrario@polimi.it</u>).

algorithms based on ECG and ABP analysis. In particular, R peaks indicative of each cardiac cycle were extracted through ECG processing, hence constructing RR intervals series (RRI); beat-by-beat series of systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), and pulse pressure (PP), computed as the difference between SBP of the current cardiac cycle and DBP of the previous cycle, were extracted from the arterial pressure waveform; beat-by-beat CVP was calculated as the mean value of continuously recorded CVP over each cardiac cycle, defined as the interval between two consecutive R peaks; the value of respiration for the each cycle was defined as the mean value of the respiration within an heart cycle.

Analyses were performed on segments of 5 minute long sliding windows, 80% overlapped. Zero-mean time series representative of short term hemodynamic variability were obtained by resampling beat-by-beat series in the time domain through an anti-aliasing low-pass filter (sampling frequency 1 Hz), and subtracting the mean value over the window.

C. Modeling autonomic control of circulation

As the mechanical ventilation produces a marked driving oscillation, the phase relationship between input and output signals of the proposed models, was found by computing the phase ϕ of cross-spectrum around 0.2Hz (frequency of the mechanical ventilator) when coherence is >0.5; the obtained value ($\phi/2\pi f$) was taken as the value of latency T.

Two models were implemented for the prediction of beatby-beat fluctuations of ABP, as an extension of a previously proposed model [3]:

$$\Delta DBP(i) = \sum_{j=1}^{n} h_{ath}(j) \cdot \Delta SBP(i-j-T_{ath}) + \sum_{j=1}^{m} h_{cpbr}(j) \cdot \Delta CVP(i-j-T_{cpbr}) \quad (1)$$

+ $h_{rr} \cdot \Delta RRI(i) + w_d(i) = DBP_{/SBP} + DBP_{/CVP} + DBP_{/RR} + w_d$
$$\Delta PP(i) = \sum_{j=1}^{p} h_{der}(j) \cdot \Delta RESP(i-j-T_{der}) + \sum_{j=1}^{q} h_{vc}(j) \cdot \Delta CVP(i-j-T_{vc}) \quad (2)$$

+ $h_{dpp} \cdot \Delta DBP(i) + w_p(i) = PP_{/RESP} + PP_{/CVP} + PP_{/DBR} + w_p$

Equation 1 models the prediction of beat-by-beat oscillations around the mean value of DBP (Δ DBP) from Δ SBP, Δ CVP and Δ RRI series, including the black box modeling of the cardiopulmonary baroreflex control of afterload resistance (DBP_{/CVP}). Equation 2 represents the prediction of beat-by-beat oscillations around the mean value of PP (Δ PP) from the variability signals of respiration, CVP and DBP, including the effects of cardiopulmonary baroreflex control of ventricular contractility (PP_{/CVP}).

The assumptions underlying this modeling approach to autonomic control of blood pressure regulation are: a) DBP is classically related to total peripheral resistance, as outlined in Windkessel modeling of the arterial tree [4]; b) PP can be employed as a surrogate of stroke volume [5]. Model components describe the following physiologic mechanisms of ABP control: arterial tree hemodynamics (DBP_{/SBP}), cardiopulmonary baroreflex control of afterload resistance (DBP_{/CVP}), diastolic runoff (DBP_{/RR}), mechanical modulation of venous return by respiration (PP_{/RESP}), effects of preload on stroke volume and cardiopulmonary baroreflex control of ventricular contractiliy (PP_{/CVP}), afterload modulation of cardiac ejection (PP/_{DBP}). Model coefficients were identified by standard system identification techniques, such as generalized least square algorithm. The noise series w_k represent residual predictions errors.

Impulse responses and step responses of the two filters $(DBP_{/CVP})$ and $(PP_{/CVP})$ are assumed to be representative of cardiopulmonary baroreflex control of afterload resistance and of ventricular contractility, while final step response values are assumed to quantify the gains of these mechanisms.

Cardiac baroreflex was investigated as well. As suggested in [6], we used a minimal closed loop model to investigate the dynamic inter-relationship between respiration, HR, and ABP. RRI fluctuations are assumed to depend on SBP fluctuations through arterial baroreflex (ABR) and a direct autonomic coupling between HR and respiration (Respiratory Cardiac Coupling, RCC). A portion of change in SBP is assumed to be produced by direct effects of the respiratory activity (DER), and by the Windkessel runoff effects (circulatory dynamics, CID)[7]:

$$\Delta RR(i) = \sum_{j=1}^{n} h_{RCC}(j) \cdot \Delta RESP(i-j-T_{RCC}) +$$

$$\sum_{j=1}^{m} h_{ABR}(j) \cdot SBP(i-j-T_{ABR}) + W_{RRI}(i)$$

$$\Delta SBP(i) = \sum_{j=1}^{p} h_{DER}(j) \cdot \Delta RESP(i-j) +$$

$$\sum_{i=1}^{p} h_{CID}(j) \cdot \Delta RR(i-j-T_{CID}) + W_{SBP}(i)$$
(4)

The impulse response of the model components (equation 3 and 4) were constructed using both Laguerre basis function [8] and the least square error method.

The baroreceptor-heart rate reflex sensitivity (BRS) was assessed through the computation of the transfer function (TF) between SBP and RRI time series in the low frequency (LF) band. The mechanical ventilation frequency higher than 0.15Hz assures that the oscillation in LF band should not be of respiratory origin [9].

D. Spectral Analysis

Autoregressive (AR) spectral analysis was performed for all ABP time series and RRI series and power in the 1) very low frequency (VLF, $0.003 < f \le 0.04Hz$), 2) low frequency (LF, $0.04, < f \le 0.15Hz$), 3) high frequency (HF, $0.15 < f \le 0.4Hz$) bands was computed, as well as 4) total power, 5) LF/HF ratio, 6) LF+HF power, 7) LF% and 8) HF% as suggested in [10].



Fig. 1. Vertical lines indicate the time of clamping and declamping. The panels report the mean values of SBP, DBP, MAP, PP, RR, CVP time series; the normalized LF component of SBP, DBP, PP variability time series; the total power and LF component of RR signal; the gain of cardiopulmonary baroreflex control of ventricular contractility (PP_{/CVP}); the gain of cardiopulmonary baroreflex control of afterload resistance (DBP_{/CVP}). When the recorded signals have several artifacts or a bad quality no indices are computed.



Fig. 2. Vertical lines indicate the time of clamping and declamping. The panels report the values of cardiac baroreflex measured with the transfer function method (TF α LF) and by the minimal model closed loop; circles indicate the gain estimated by the least square error method, triangles by the Laguerre basis function (LBF) expansion.

III. RESULTS

As figure 1 shows, the effects of drug infusion are clearly observable in the LF spectral components. Before clamping and after declamping the sympathetic nervous system (SNS) drastically decreases and increases respectively (about a factor of fourfold or more) due to vasodilators and vasoconstrictors. After the first minutes following declamping, the response of the analyzed patients is mainly volume and drug driven: the increase of venous return, as shown by a significant raise of CVP, is accompanied by an increase of HR, of LF oscillations in ABP signals, and of total power of HR (Fig.1). After this transient, the phase after declamping is characterized by i) the increase of PP_{/CVP} gain which becomes positive again, as it is in baseline ii) the increase of DBP_{/CVP} gain which becomes negative again (Fig.3).

The recovery after the transient seems to be mainly mediated by cardiopulmonary baroreflex more than cardiac baroreflex. As the values of cardiac baroreflex are quite stable and low during the procedure and no remarkable trends were obtained in the analyzed subjects (Figure 2).



Fig. 3. Values of cardiopulmonary baroreflex control of ventricular contractiliy ($PP_{/CVP}$), obtained from the 4 subjects are showed for the three different phase.

IV. DISCUSSION AND CONCLUSION

In this paper we present preliminary results, showing the potential of investigating autonomic nervous system control of circulation under anesthesia in aiding hemodynamic monitoring and maintenance of blood pressure stability in patients undergoing major surgery.

While these results provide with a preliminary picture, future works should aim at characterizing the hemodynamic status of patients in the perioperative period and recast the results in form of synthetic indexes and/or indicators. The integration with modeling techniques suited to interpret variability of central volumes and to track heart performance under stress conditions such as anesthesia and surgery can pave the way to the definition and validation of clinical tools designed to support the decision making of anesthesiologists, constantly faced with the challenge of identifying the optimal strategy to stabilize volumes and pressures during surgery.



Fig. 4. Mean values of SBP, DBP, MAP, PP, HR and CVP obtained from the 4 subjects are showed for the three different phase.

References

- S. Akselrod, et al., "Power spectrum analysis of heart rate fluctuation: a quantitative probe of beat-to-beat cardiovascular control," Science, vol. 213, no. 4504, pp. 220-222, July 1981
- [2] M. Pagani, et al., "Power spectral analysis of heart rate and arterial pressure variabilities as a marker of sympatho-vagal interaction in man and conscious dog," Circ. Res., vol. 59, no. 2, pp. 178-193, Aug. 1986.
- [3] F. Aletti, T. Bassani, D. Lucini, M. Pagani, and G. Baselli, "Multivariate decomposition of arterial blood pressure variability for the assessment of arterial control of circulation," IEEE Trans. Biomed. Eng, vol. 56, no. 7, pp. 1781-1790, July 2009.
- [4] Mukkamala R, Reisner AT, Hojman HM, Mark RG, Cohen RJ. Continuous cardiac output monitoring by peripheral blood pressure waveform analysis. IEEE Trans Biomed Eng. 53(3):459-67, 2006
- [5] X. Xiao, et al., "Effects of simulated microgravity on closed-loop cardiovascular regulation and orthostatic intolerance: analysis by means of system identification," J. Appl. Physiol, vol. 96, no. 2, pp. 489-497, 2004.
- [6] Khoo MC, Modeling of autonomic control in sleep-disordered breathing. Cardiovase Eng. 8(1):30-41, 2008.
- [7] A. Blasi, et al., "Autonomic cardiovascular control following transient arousal from sleep: a time-varying closed-loop model," IEEE Trans. Biomed. Eng, vol. 53, no. 1, pp. 74-82, Jan. 2006.
- [8] Marmarelis VZ. Identification of nonlinear biological systems using Laguerre expansions of kernels. Ann Biomed Eng ;21(6):573-89, 1993.
- [9] Pinna GD, Maestri R, et al.. Applicability and clinical relevance of the transfer function method in the assessment of baroreflex sensitivity in heart failure patients. J Am Coll Cardiol, 46(7):1314-21, 2005.
- [10] "Heart rate variability: standards of measurement, physiological interpretation and clinical use". Task Force. *Circulation*, vol. 93, pp. 1043-1065, 1996.