Cardiovascular Function Monitoring in Critical Care

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Abstract— This paper presents a brief overview of the main applications of methods and models for the assessment of cardiovascular regulation by the autonomic nervous system to critical care settings. In particular, findings inherent to the investigation of the hemodynamic alterations induced by anesthesia and fluid challenge as a countermeasure to intraoperative hypotension and hemodynamic instability, and by hemodialytic treatments are discussed. Standard heart rate variability and arterial blood pressure variability analyses were carried out, based on spectral methods and multivariate prediction models for the description of the main time domain and frequency domain properties of neural control systems of circulation. The novelty of this work is represented by the field of application of relatively well established techniques. The importance of such approaches is manifold as emphasized in the paper, and it relies on: i) the insight into the functioning and potential impairment of the neural and reflex control of arterial blood pressure, ii) the characterization of hemodynamic stability at the system level, and iii) the potential applications for monitoring purposes, which may guide preventive and therapeutic strategies to counteract life threatening injuries.

I. INTRODUCTION

Cardiovascular (CV) variability (CVV) has long been studied to assess autonomic nervous system (ANS) control of circulation, and several analysis and modeling techniques have been developed over the last three decades (Akselrod et al. 1981, 1985; de Boer et al., 1985; Pagani et al., 1986; Saul et al., 1991) to disentangle the manifold mechanisms contributing to overall regulation of heart rate and blood pressure. Linear and non linear approaches (Goldberger, 1990), either mono- and multi-variate (Baselli, 1988; Jo et al, 2007; Blasi et al., 2006; Aletti et al., 2009; Mukkamala et al., 2006a, 2006b) both in the time and frequency domains, can extract and characterize the information inherent to the short term control of heart rate (HR), arterial blood pressure (ABP), and volemia on a beat-by-beat basis.

Along the same lines, the mathematical analysis of peripheral and central ABP waveforms, and of the main parameters of the arterial tree, has inspired the development of system identification techniques for the estimation of variables such as cardiac output (CO), aortic blood pressure, intracranial pressure (ICP) (Mukkamala et al., 2006a, 2006b; Sun et al, 2009). Such variables cannot be continuously measured or are very hardly accessible, even in severely injured patients; still, the information carried by these signals is instrumental to gain an insight on the correct functioning of the CV system and its control systems or the level of injury in critically ill patients.

Although heart rate variability (HRV), and blood pressure variability (BPV) convey a powerful diagnostic meaning (e.g., fetal heart rate variability study for the discrimination of intra uterine growth restricted fetuses (Ferrario at al., 2006, 2009)), and have been the focus of a large number of physiologic studies, where a wide array of conditions were taken into consideration (e.g. exercise, simulated microgravity, simulated orthostatic stimuli, simulated hemorrhage, interaction between respiratory dynamics and cardiovascular dynamics, etc.), not as many results have been published on the autonomic control of circulation in critical care settings.

Two clinical conditions where a deeper insight into the mechanisms which determine ABP control is necessary, are surgery and hemodialysis (HD). One of the main goals of physicians dealing with patients management undergoing surgery or HD is to prevent hypotensive episodes which might hamper an adequate perfusion of organs, with an impact on mortality and comorbidities (Wizemann, 2009).

In this paper, an overview of the approaches adopted to analyze hemodynamic stability is presented, with an emphasis on the potential relevance of assessing autonomic control of circulation in supporting clinical decisions to predict and prevent hypotension.

A. Intraoperative monitoring of hemodynamic stability

CV disease is the primary cause of death world-wide with different forms of hypertension taking the lion's share. An extremely high co-morbidity with respiratory malfunctions such as chronic obstructive pulmonary disease (COPD) reveals an intimate connection between the CV and respiratory system, and their control systems. This association is particularly relevant in patients undergoing surgery and requiring mechanical ventilation, where hemodynamics can be either supported or strongly compromised by the choice of the ventilation strategy.

The prevention of adverse CV and cardiorespiratory events such as hypotension, ischemia and pulmonary oedema, and the choice of therapeutic interventions and strategies aimed at guaranteeing organ perfusion and haemodynamic stability, can only be performed acutely under the guidance of informative, integrated intra-and perioperative patient monitoring systems.

The maintenance of physiological homeostasis during surgery, as well as the potential blunting of reflex and compensatory responses to external perturbations due to anesthesia clarify the importance of assessing CVV and
ANS control of circulation. The well established methodological and patho-physiological knowledge on CVV analysis can shed light on this problem and constitute a novel field of application for techniques which have been successful in several areas.

**B. Autonomic nervous system control of cardiovascular variability in hemodialysis patients**

Fluid overload (FO) is an important and independent predictor of mortality in chronic HD patients (Wizemann, 2009) and, together with hypertension, it is known to be a highly relevant precursor to the development of left ventricular hypertrophy in HD patients (Ronco, 2008). In order to manage ABP and hydration in these subjects, understanding the different responses to dialysis treatments requires the assessment of the ANS control of CVV in order to test the hypothesis that hypertension in the renal failure population is volume dependent. This hypothesis has revealed major flaws, though. The classification suggested in (Wabel, 2008) highlights that there are patients who are hypertensive but not overhydrated, and patients who are not hypertensive but overhydrated. Since HRV is a well known measure of the ANS regulation of ABP and volumes, its use in the analysis of ECG recordings of patients routinely undergoing HD can represent a novel field of application of techniques and models for assessing CVV, with the potential of supporting the care of patients with a limited quality of life due to an unstable control of ABP.

**II. METHODS**

**A. Intraoperative monitoring of hemodynamic stability**

In this paper, a case study of the cardiopulmonary baroreflex (CPBR) control of ventricular contractility and afterload in a 61 year old patient undergoing routine surgery for prostate cancer removal will be presented. Arterial and venous pressures, recorded at 100Hz, respectively with an arterial catheter inserted in the brachial artery and a venous catheter placed in the superior vena cava, ECG (250 Hz) and respiration (25 Hz) were pre-processed in order to select ~300 s long, artifact free, stationary segments and to extract the beat-by-beat variability series of RR intervals (RRI); systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), pulse pressure (PP), central venous pressure (CVP), and respiration (RESP). Normalized, zero-mean time series were subsequently obtained by downsampling to 0.5 Hz the beat-by-beat series by means of an anti-aliasing low-pass filter, and by subtracting and dividing by the mean.

Two black box models for the estimation of the gains of the CPBR control of afterload (1) and of ventricular contractility (2), based on invasive measurements of ABP and CVP were proposed (Toschi et al., 2010):

\[
DBP(i) = \sum_{j=1}^{n} h_d(j) \cdot SBP(i-j) + \sum_{j=1}^{m} h_u(j) \cdot CVP(i-j) + h_u(j) \cdot RR(i) + w_d(i) = DBP_{SBP} + DBP_{CVP} + DBP_{RR} + w_d
\]

\[
PP(i) = \sum_{j=1}^{p} h_q(j) \cdot RESP(i-j) + \sum_{j=1}^{a} h_q(j) \cdot CVP(i-j) + h_q(j) \cdot DBP(i) + w_p(i) = PP_{RESP} + PP_{CVP} + PP_{DBP} + w_p
\]

DBP variability was predicted by: mechanical responses of the arterial tree (DBP_{SBP}), CPBR control of afterload resistance (DBP_{CVP}), diastolic runoff (DBP_{RR}); PP variability by: cardiorespiratory modulation of venous return (PP_{RESP}), effects of preload on stroke volume and CPBR control of ventricular contractility (PP_{CVP}), afterload modulation of cardiac ejection (PP_{DBP}). The model coefficients were computed by standard system identification techniques. The noises \( w_d \) and \( w_p \) represent the residual errors on the predictions.

The gains of the CPBR control of total peripheral resistance and of ventricular contractility were computed as the final values of the step responses of the two filters accounting for these mechanisms (DBP_{CVP} and PP_{CVP}) before and after a “fluid challenge” maneuver. The key issue that was meant to be addressed by this analysis was to provide a quantitative assessment of the effectiveness of intravenous (IV) infusion in restoring blood pressure by increasing the CPBR gains as a countermeasure to a decreased mean arterial pressure.

**B. Autonomic nervous system control of cardiovascular variability in hemodialysis patients**

The aim of the analysis presented in this paper was to investigate the relationship between FO and the autonomic response to the HD treatment. 39 patients aged 60-80 yrs were recruited from the dialysis unit of San Bortolo Hospital, Vicenza (Ferrario et al., 2010). 24 hr ECG Holter recordings (sampling rate 250 Hz) were collected starting immediately before the dialysis treatment. Before each HD treatment, FO was assessed by whole body bioimpedance spectroscopy, which provided the FO expressed in liters (Chamney, 2007). The patients were classified in four groups according to FO values and the systolic blood pressure (SBP) measured before HD:

- **Group I:** patients with a FO >2.5l and SBP >140 mmHg.
- **Group II:** patients with a FO>2.5l and SPB<140 mmHg.
- **Group IV:** patients with a FO>2.5l and SBP<140 mmHg.
- **Group D+N:** patients with -11<FO<2.5l and 100 mmHg < SBP < 150 mmHg. This region is commonly associated to healthy subjects or to dialysis patient before HD treatment in a well managed ESRD condition (Wabel, 2008).

Approximately 5 minute long corrected beat-by-beat series of normal-to-normal beats (NN) intervals were resampled at 2Hz, and analyzed during the first and the last 30 minutes of HD, the first hour after HD, and during the
night (12.00 p.m.-4 a.m.).

Autoregressive (AR) spectral analysis was performed and power in the 1) very low frequency (VLF, 0.003-0.04Hz), 2) low frequency (LF, 0.04-0.15Hz), 3) high frequency (HF, 0.15-0.4Hz) bands was computed, as well as 4) the LF/HF ratio (Task Force, 1996). Moreover, we computed: the mean NN interval, the standard deviation of the NN intervals (SDNN), the percentage of pairs of adjacent NN intervals differing by more than 50 ms in the sequence (pNN50%), the square root of the mean of the sum of the squares of differences between adjacent NN intervals (RMSSD), the standard deviation of differences between adjacent NN intervals (SDSD) (Task Force, 1996).

III. RESULTS

A. Intraoperative monitoring of hemodynamic stability

The changes in the gains of the CPBR control of afterload (fig. 1) and of contractility (fig. 2), before and after a fast IV infusion following a hypotensive episode, suggested that the CPBR was sensitive to the increase in CVP due to the fluid administration: the gain of the total peripheral resistance control became negative and its absolute value increased, while the gain of the contractility became positive and its absolute value was increased. Both these trends were consistent with the typical responses of the CPBR following a positive variation in CVP.

B. Autonomic nervous system control of cardiovascular variability in hemodialysis patients

The selected patients had an average ultra filtration rate (UFR) higher than 0.5l/hr and belonged to group I (16 patients), group IV (11 patients), and group Dx+N (12 patients). We obtained significant differences during night: i) SDSD resulted significantly higher for Group IV with respect to Group I and Group N+Dx; ii) RMSSD and iii) pNN50% resulted significantly higher for Group IV with respect to Group N+Dx. SDSD interquartile values of Group I: 44.41 (12.68, 57.17) ms; Group IV: 109.14 (21.19, 182.7) ms; Group N+Dx: 34.27 (12.73, 49.58) ms; RMSSD interquartile values of Group I: 1152 (582, 1883) ms²; Group IV: 2361 (666, 4184) ms²; Group N+Dx: 762 (452, 1581) ms². pNN50% interquartile values of Group I: 3.07 (0.68, 8.45); Group IV: 9.17 (0.27, 34.42); Group N+Dx: 1.4 (0.13, 8.00).

The spectral HF component resulted significantly higher for Group IV with respect to Group N+Dx and Group I when computed 1hr after HD (Figure 3). The raise in HF power following HD in the group IV patients suggested an increase in the parasympathetic tone of these patients. In particular, this result could justify the hypothesis that an elevated FO may produce two different conditions: a) an increase in blood pressure according to the rationale of volume-dependent hypertension (group I) b) an enhanced vagal tone (group IV).

Fig. 1: Step responses of the cardiopulmonary baroreflex control of afterload resistance before and after fluid challenge

Fig. 2: Step responses of the cardiopulmonary baroreflex control of ventricular contractility before and after fluid challenge

Fig. 3: HF(ms²) power of RRI variability calculated 1 hr after the hemodialysis treatment. In green is group I (16 patients), in red group IV (11 patients), and in blue group Dx+N (12 patients).

IV. CONCLUSION

In this paper a brief overview of the current applications of standard techniques for the model identification of cardiovascular control and for the assessment of heart rate and hemodynamic variability to critical care applications was given. Autonomic nervous system control is “in competition” with the mechanical phenomena of fluid balance in conditions where the working point of the circulation may be significantly shifted from the physiologic range of operations. End stage renal disease and the hemodialytic treatment, as well as anesthesia, or for
instance other conditions such as intensive care, trauma, hemorrhagic shock, sepsis, etc., have a severe effect on stressed and unستressed fluid volumes and volumes. This might affect the levels of mean pressure, venous return and stroke volume, and the perfusion of organs might be in danger. During surgery requiring the intubation of the patient, the overall functioning of circulation is further put in jeopardy by mechanical ventilation, which strongly alters the respiratory patterns, mainly because of the intrathoracic positive pressure forced by the ventilator.

Although the root cause for the overall impairment of physiologic cardiovascular regulation is the product of lower scale mechanisms (Schmid-Schönbein, 2008) and fundamentally entails a diffuse, systemic inflammatory state, the role of ischemia and reperfusion is key in triggering potentially life threatening phenomena. Therefore, the importance of the approach presented in this paper consists in the capability of providing an in-depth insight into the contribution of the autonomic nervous system function in the compensation to critical injuries, analyzed from an organ and system level perspective. The assessment of the potential impairment of the autonomic control of circulation may prove helpful in guiding the therapeutic choices of physicians following a correct prediction of a potentially harmful hypotensive episode.

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REFERENCES


