Computer models in bedside physiology

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Chapter 7
Summary and general conclusions

Introduction

Computer modeling in bedside physiology may assist clinical research, in cases where:
1. It is impossible to perform the experiments in reality;
2. It is difficult to repeat the observation in the same condition;
3. It is expensive to do the experiment;
4. It offers a new angle to analyze the problems.

Modeling and simulation can be used to simulate clinical situations, and to offer a virtual platform to solve clinical problems. Our circulation model for Cardiopulmonary Resuscitation (CPR) is an example; to compare the effects of various CPR techniques on the same subject is impossible; apart from the obvious ethical issues, to experiment on animals is expensive and it is difficult to imitate the situation in humans. Comparing CPR techniques in a circulation model can avoid these disadvantages and offer an unbiased platform.

In Chapters 2 and 3 we used a circulation model to compare the effects of different CPR techniques, and to investigate the potential risks of intensive CPR performance. In Chapter 6 we used a circulation model with Autonomic Nervous System (ANS) adjustment to simulate volume loss and infusion, to check whether pulse pressure variation (PPV) might reflect fluid responsiveness.

The ANS is an important control system, which affects heart rate, blood pressure and –indirectly- respiratory rate, to name but a few. Some diseases influence the function of the ANS and vice versa, ANS dysfunction may also influence someone’s health. Analysis of physiological signals like blood pressure variability (BPV) and heart rate variability (HRV) can detect the ‘status’ of the ANS, to dig deeper into hidden pathology.

Chapter 4 is about Chronic Heart Failure (CHF) patients who are on beta-blocker treatment; if hospitalized, even with all monitors around, they might still slip into a sympathetic state without any (early) alarm sounding. We analyzed heart rate variability (HRV) in several ways, testing newly proposed techniques, to find which one would be able to give an early warning and uncover hidden risks.
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Another example is the Brugada syndrome (BrS), which is a genetic disease which might lead to sudden death, even with normal cardiac structure. The problem is that some patients may have a high risk, some don’t. How to recognize those who are at risk is important but difficult. In Chapter 5 we applied extensive analysis to evaluate the ANS function in recordings which had been made by clinical colleagues who asked BrS patients to remain quietly supine for 10 minutes and then stand up for another 10 minutes, all while recording continuous BP and HR.

Summary of findings

**Question 1:** Which cardiopulmonary resuscitation technique will improve cardiac output best?

In Chapter 2 we used a ‘stopped’ cardiac circulation model, to compare the effects of five CPR techniques: chest-only compression CPR (CO-CPR), Active compression-decompression CPR (ACD-CPR), Interposed abdomen compression CPR (IAC-CPR), Lifestick CPR, and Enhanced External Counterpulsation CPR (EECP-CPR)). In the circulation model, Lifestick-CPR gave the best cardiac output, coronary perfusion, and cerebral perfusion. At the same time we found that it is very important to improve CO by combining chest compression and abdomen compression, so if cardiac arrest occurs out-of-hospital, IAC-CPR is recommended because it can be performed without equipment by two rescuers working together.

**Question 2:** If we can improve cardiac output by these alternative CPR techniques, why is chest-compression CPR still the only CPR mode that is recommended in the Guidelines?

In Chapter 3 we refined our look at cardio-pulmonary resuscitation: we measured not only CO, perfusion to all important organs, but also pulmonary pressure. We found that all combined efforts to improve CO might put the lungs at risk to develop acute edema. That is possibly why CO-CPR still stands out as ‘treatment of choice’, chosen above alternative CPR techniques. To create a large perfusion volume a big volume of blood is accumulated in the chest. But then we have to use high pressure to push the blood to where it is needed. In this process, if the lungs are connected both to the vascular pressures on one side and to outside air on the other, the exerted high pressure can lead to pulmonary edema. A solution would be, when performing CPR in this way, to apply positive pressure ventilation avoiding this lung pressure difference, or, alternatively, compression pressure should be controlled to within tolerance levels to protect the lungs.

**Question 3:** Can pulse pressure variation (PPV) predict fluid responsiveness?
In Chapter 6 we tested the relation between PPV and blood volume change in test subjects and a computer model. We confirmed that under anesthesia PPV is a good reflection of cardiac filling (in healthy hearts). In the conscious state PPV is more variable: we need a long observation period to calculate PPV, to reflect fluid responsiveness. In the conscious state PPV is under the influence of many disturbances other than changes in cardiac filling as is reflected by Fourier analysis of its variability.

**Question 4:** Which HRV parameters can detect quickly when a CHF patient slips into a sympathetic state, even under beta-blocker treatment?

In Chapter 4 we used the standing condition to induce a more sympathetic situation (compared to the supine state). Among all HRV parameters (meanIBI, SD-IBI, rMSSD, LF, HF, LF/HF, MSV, MSD) only meanIBI, rMSSD, pIBIS0, and MSD were still able to detect the change between supine and upright state. This ruled out a set of newly proposed analysis techniques for monitoring in acutely ill patients.

**Question 5:** Can we discriminate the ANS in BrS patients from healthy subjects by applying physiological parameter analysis? In what way they are different?

In Chapter 5 we compared a wide range of cardiovascular parameters between healthy controls and BrS patients; in the supine state it is hard to tell any difference between the two groups. When the sympathetic nervous system is challenged by a position change from supine to standing, we found that there is probably less sympathetic outflow increase in BrS subjects, which might lead to vasovagal syncope, or even carry a potential VF risk.

**Limitations**

To concentrate on the main problem: the model is always a simplification of the real situation. In reality the patients’ situations are complex; in Chapters 2 and 3 we simulated the ‘stopped’ circulation; we have to ignore all kinds of possible effects like oxygenation, blood flow inertia, the effects of CNS. In the model we set parameters as constant, in reality they may be changing with pressure and with time; our model is limited to simulate a standard 70kg man, in reality only few patients fit this pattern. In Chapter 6, although we got a more individualized model, we neglected long-term adjustments, like circulating hormones.

In the Chapters 2, 3 and 6 we do not have parallel clinical or animal experimental results to compare to the results of our modeling.
In Chapter 4 we only got short heart rate recordings (2 x 10 min); to get more stable values for the ‘modern’ chaos parameters like MSE, MSV and MSD we should extend the test period longer (15-20min) and in future experiments a sympathetic state shift might be induced slower and more continuous (like on a tilt table in slow mode). This could be more like a realistic clinical situation. In Chapter 5 we need more healthy controls and BrS patients in different age group, to verify the experimental results.

General Conclusion

Even with all the limitations, to solve clinical problems by way of physiological modeling and biomedical engineering is not rare any more. It is a fast growing field, as it gives the opportunity of ‘another angle’ to look at and analyze the problems at hand. However without a full understanding of the medical problems to be obtained by cooperation with clinicians, biomedical engineering is only ‘armchair strategist’ science. As biomedical engineers, we just hope that clinicians, who are with so much knowledge of practical medical problems, can open their arms, to welcome these kinds of ‘healthy’ cooperations.