Non-invasive Assessment of Hemodynamics in Adolescents with Arterial Tonometry and Doppler Ultrasound during a Conventional Stress Test

K Matthys[1], D Vanhercke[2], S Van Aken[3], K De Groote[3], I Coomans[3], P Verdonck[1]

[1]Hydraulics Laboratory-IBITECH-Ghent University [2]Cardiology Dept., General Hospital St. Lucas
[3]Pediatric Cardiology Dept., Ghent University Hospital, Ghent Belgium

Abstract

Aiming to improve early diagnosis of people at cardiovascular risk, we are developing a custom set-up to allow an adequate hemodynamic analysis of heart function and arterial circulation properties, based on non-invasive acquisition of pressure (arterial tonometry) and flow (Doppler ultrasound techniques) waveforms.

In an experimental setting 15 healthy volunteers were examined on a custom made supine bicycle. Able to record usable data throughout the bicycle test and automatically analyse derived hemodynamic parameters such as compliance, peripheral resistance, etc., we also applied the set-up in a real clinical environment.

This research contributes to a more complete cardiovascular examination without significant additional discomfort for the patient or prolongation of the test protocol.

1. Introduction

The analysis of the cardiovascular system at early age has an increasing social interest. Over the years, a lot of attention has been paid to the assessment of causes of atheromatosis (blood vessel degeneration). Several risk factors were clearly delineated, such as lack of physical exercise, smoking, and diabetes. Methods that can identify people at risk - in a stage before the pathological process causes irreversible damage – are important from prevention point of view.

Therefore, in this research project our main focus during in vivo experiments lies on adolescent subjects. Moreover, in this age group observations of risk factor repercussion are not yet interfered by any pathological damage.

Aiming to improve an early diagnosis, we are developing a set-up for the adequate hemodynamic analysis of heart function and arterial circulation properties by using arterial tonometry [1] and Doppler ultrasound techniques, not only for use in rest conditions but also during stress tests. These non-invasive techniques are comfortable for the examined subjects and allow routine application.

Quantifying the properties of heart and blood vessels is possible by the assessment of hemodynamic parameters such as peripheral resistance, arterial compliance, etc. Calculation of these parameters can be done in real-time provided that three signals are simultaneously available: heart rate, blood pressure and blood flow waveforms. The development of a diagnostic set-up allows acquiring these three non-invasively measured signals in a synchronized way from separate medical devices. These time-varying signals will be visualized in real-time and derived hemodynamic parameters will be calculated automatically.

2. Experimental setting

2.1. Methods

To examine the feasibility of acquiring signals continuously while the subject is performing a stress test, 15 healthy volunteers (10 male and 5 female, age: 23.2 +- 3.7) were asked to cycle on a custom made supine bicycle in an experimental setting at the Hydraulics Laboratory.

Figure 1: Supine stress test at the Hydraulics Laboratory on a custom made bicycle.

Tonometric pressure data was recorded on the right radial artery, with a cuff calibration on the opposite arm, and Doppler flow recordings done in a suprasternal position. The load level was augmented every 3 minutes (step protocol, with a maximum of 8 levels), while cycling was done at a constant speed of 20 km/h. During exercise, an ECG recording, the pressure signal of a tonometric pen probe (SPT-301, Millar Instruments™) placed on the radial artery and the Doppler spectrogram, automatically derived by the set-up from the audio signal of a Doppler device (800CFM, GE Vingmed™), were simultaneously acquired from the separate devices and visualized in real-time on one computer, and then processed with a custom written program (SAM, © S. Carlier), already used for previous studies in resting conditions. The tonometric probe as well as the Doppler probe was held manually in position during the readings.

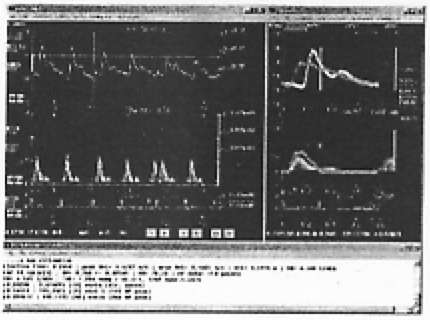

Figure 2: Screen print of the custom written program (SAM, © S. Carlier) used for data analysis. Tonometric pressure data, Doppler flow recordings and ECG is shown on the left. Same signals averaged over 1 heart cycle are shown on the right.

As a tonometer only gives information on the *waveform*, and does not provide absolute values, a calibration for the pressure waveform is necessary. This was obtained by an automatic cuff-device for domestic use (Blood Pressure Watch, Nais™), applied at the opposite radial artery. A calibration measurement was done at the beginning of each load level, thus providing systolic and diastolic blood pressure values.

Pressure and flow waveforms are required at the very beginning of the vascular tree (i.e. at the site of the aortic valve). As pressure cannot be acquired non-invasively at this site (flow can by the Doppler technique), transformation of a peripheral blood pressure waveform (non-invasively measured with the tonometer) to a central aortic pressure waveform was (automatically) done by use of a transfer function. With this information, parameters such as arterial compliance, peripheral resistance, aortic impedance, stroke volume, cardiac output etc. were finally calculated.

2.2. Results and discussion

The number of subjects (from a total of 15) for which the calibration values could be obtained as higher load levels were reached, drops fairly quick from 11 subjects at 9 minutes of exercise (load level 4) to only 2 subjects at load level 8, due to instable readings from the cuff calibration device (table1, Cuff). Therefore, we decided only to investigate the signals measured during the first three load levels, thus looking solely at moderate stress activity.

As signal quality from the tonometric pen probe is very sensitive to motion artefacts, it became less feasible with higher load levels to find and stabilize a correct position for the probe on the radial artery and record a sufficient amount (i.e. 10 to 15) of heart cycles within the 3 minute timeframe of one load level. At load level 3 (6 minutes of cycling), calibration and signal quality of blood pressure, flow and ECG, were still good in 8 of 15 subjects (table 1, Cycles).

Table 1. Number of subjects (from a total of 10 Male and 5 Female) for whom calibration (Cuff) and signal quality (Cycles) were still good for a specific load level (Lx).

Load level	L0 1	L3 2	L6 3	L9 4	L12 5	L15 6	L18 7	L21 8
Cuff	15	14	14	11	10	7	5	2
Cycles	13	11	8					
Female	3	2	1					
Male	10	9	7					

For these 8 subjects hemodynamic parameters were calculated off line, with an emphasis on resistance and compliance values. Results are shown in figure 3 and 4.

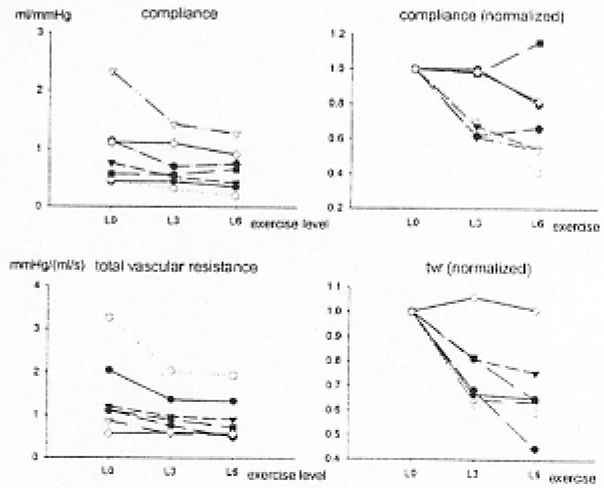

Figure 3: Compliance and total vascular resistance (left) also normalized to their value at load level L0 (right).

As the values for total vascular resistance and compliance varied quite a lot amongst different subjects, they were also normalized to their value at load level L0.

A measure for maximal compliance is estimated by using the ratio of stroke volume to pulse pressure (difference between systolic and diastolic pressure), and a measure for the amount of damping that waveforms undergo in the vascular tree is given by a time constant Tau, defined as resistance times compliance (figure 4).

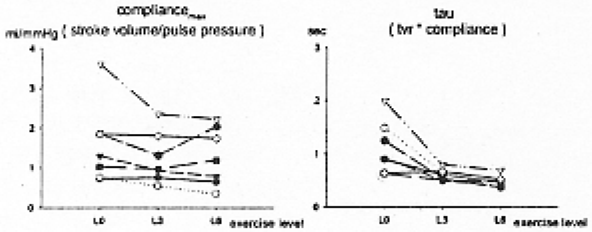

Figure 4: Values for $compliance_{max}$ defined as the ratio of stroke volume to pulse pressure (left), with time constant Tau defined as resistance times compliance (right).

As far as real quantification is concerned these results are definitely limited, because of the small number of subjects and the practical drawbacks, which occurred concerning calibration and raw signal quality. Nevertheless, already a fairly good indication of the change of these examined hemodynamic parameters during stress activity was obtained in a fast and non-invasive way, clearly demonstrating the potential for such a set-up and protocol in a real clinical environment.

3. Clinical setting

3.1. Methods

We applied the set-up in a clinical environment on a 17-year old patient with diabetes, coming in for a routine diagnostic stress test.

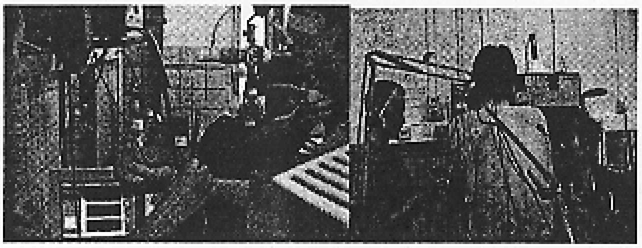

Figure 5: Clinical setting at the exercise laboratory of the pediatric cardiology department.

A standing bicycle was used with a ramp protocol (start: 0 Watt, slope: subject weight in kg/4 = W/min: e.g. 60kg=15W/min) together with a more specialized cuff calibration device on the brachial artery intended for use during stress tests (inflating again every 3 minutes). Breath-by-breath gas analysis was also performed to calculate VO_2 max.

3.2. Results and discussion

Although a standing bike generates more motion artefacts to the sensitive tonometer probe and the upright cycling position is less optimal for Doppler image assessment, we succeeded in acquiring pressure and flow waveforms every 3 minutes throughout the whole exercise test (peak exercise level was reached at 15 min, Max power: 240 Watt, heart rate: 204 bpm, max sbp/dbp: 223/35 mmHg, VO2 max: 42.1).

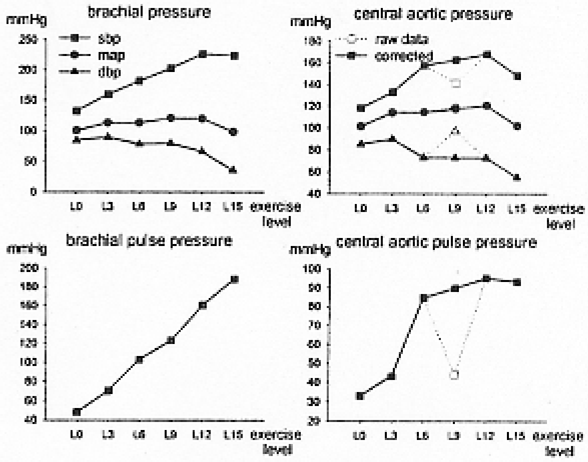

Figure 6: Measured peripheral (left) and calculated central aortic (right) pressure values.

Figure 6 shows the calibration values for blood pressure. Hemodynamic calculation requires the use of the central aortic pressure; therefore it is derived with a mathematical transformation from pressure at a peripheral site. As derived aortic values showed an extreme outline value at load level L9, which after examination was due to the poor quality of the tonometer pressure data at that level, all parameters at level L9 were replaced by an average value of level L6 and level L12 (raw data vs. corrected, figures 6 and 8).

Both measured as derived pressures show an increasing systolic blood pressure and slightly decreasing diastolic pressure, thus an increase of pulse pressure during exercise.

While figure 7 shows the expected increasing slope of blood flow and cardiac output with exercise, we mainly focused again on resistance and compliance parameters (figure 8). Compliance was measured in three different ways: the pulse pressure method [2] and the area method [3], for which again two variations were used (differing by the fact that integration during calculation is done over a different part in time of the heart cycle: 'area end' uses the 'dicrotic notch to end diastole' interval, while 'area all' uses the whole heart cycle).

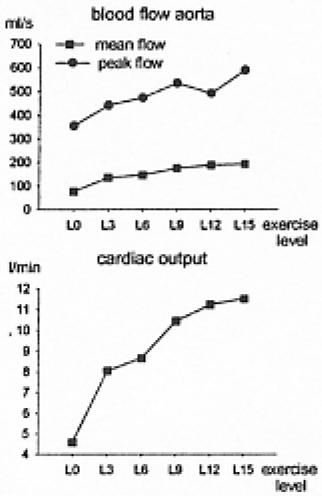

Figure 7: Blood flow and cardiac output values.

Peripheral resistance (figure 8, upper left) showed a clear decline in an almost linear way (from 1.33mmHg.s/ml in rest to 0.53mmHg.s/ml at peak exercise) with an average drop of 0.16mmHg.s/ml every 3 min.

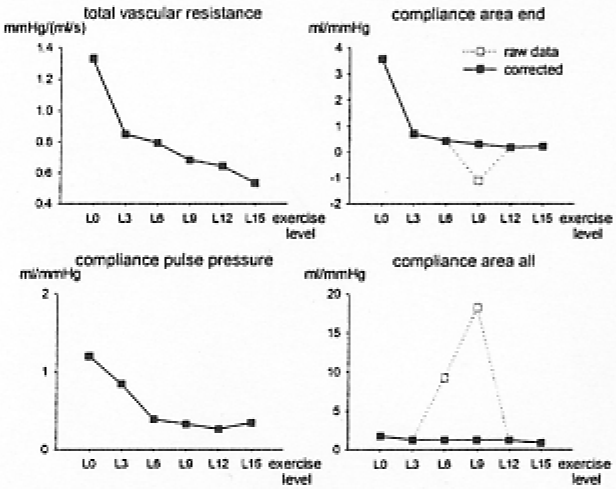

Figure 8: Total vascular resistance and compliance.

Arterial compliance with pulse pressure method (figure 8, lower left) dropped in more of an exponential way (from 1.19ml/mmHg in rest to 0.34ml/mmHg at peak exercise). Compliance at maximum exercise appeared 4 times lower than in rest.

The results also showed that use of the area method is less appropriate than the pulse pressure method, because it appeared more sensitive to artefacts introduced by the mathematical transformation of pressure (with transfer function) or to poor quality of the raw signals data. This is clear by the extreme outline values shown on figure 8.

4. Conclusion

First, these experiments have taught us that an experienced operator is necessary for handling the tonometric and Doppler probes. Especially the non-invasive pressure measurement requires a lot of attention. Perhaps a hands-free tonometer using a wrist fixation (e.g. Colin Instruments™) could be an improvement, but it is also far more expensive. Also, a very reliable calibration device is imperative.

Looking more at the computational point of view, more efforts are necessary on the level of the mathematical transformation from peripheral to central aortic pressure. Another study currently running at the Hydraulics Laboratory will compare and investigate the effects of different transformation methods, especially looking at the more recent technique of autoregressive exogenous modelling versus classical Fourier analysis.

Nevertheless, this research has already demonstrated the feasibility of adding extra hemodynamic information to a routine diagnostic investigation by the combination of simple non-invasive techniques such as an ECG, Doppler and tonometer device, and these results contribute to a more complete cardiovascular examination without significant additional discomfort for the examined subject or prolongation of the test protocol.

Acknowledgements

Thanks to Stéphane Carlier for the use of his electronic equipment and especially to Tine De Backer for her unexpected help in the hospital although in a very pregnant condition.

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Address for correspondence.
Koen Matthys, MScME
IBITECH-Hydraulics Lab-Ghent University
Sint-Pietersnieuwstraat 41 B-9000 Ghent - Belgium
Voice: +32 9 264 89 26 Fax: +32 9 264 35 95
E-mail : koen.matthys@rug.ac.be