A Pilot Study of Photoplethysmographic Peripheral Pulse Transit Times in Paediatric Heart Transplant Recipients and Healthy Children

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Abstract

Previous studies have demonstrated increased arterial stiffness (AS) in paediatric heart transplant recipients (HTR) by using established SphygmoCor technology.

The aim of this study was to assess pulse transit times at three different peripheral body sites in HTR, and in comparison to healthy controls, by using relatively low-cost and easy-to-perform photoplethysmography (PPG) technology.

PPG waveforms and an electrocardiography timing reference were recorded from 12 HTR (age range 8-17 years; 5 males) and 30 healthy children (age range 8-16 years; 15 males) from the right and left ear lobes, index fingers, and great toes. The median values for pulse transit times to PPG-pulse foot (PTTf) were calculated over a period of 60 heart beats, with right and left sides averaged at each segmental site.

Toe PTTf was significantly shorter in HTR (median 290 ms) compared to controls (324 ms, $p < 0.05$). No significant differences were found for ear and finger PTTf. Furthermore, toe PTTf significantly correlated with subject height both in HTR ($\rho = 0.78$, $p < 0.01$, slope = 88 ms/m) and controls ($\rho = 0.76$, $p < 0.001$, slope = 132 ms/m).

A shorter PTTf at the toe site is consistent with increased AS in paediatric heart transplant recipients and the results from correlation analysis further corroborated this finding.

1. Introduction

A heart transplant is a potential option for children with severe heart failure and is associated with a significant improvement of life expectancy [1]. In children who survive transplantation there are a number of factors which can affect graft longevity, the most important of which are rejection, coronary artery disease, and arterial hypertension.

Arterial hypertension in paediatric heart transplant recipients (HTR) is relatively common and is multi-factorial in origin [2]. A previous study from our group [3] showed that arterial stiffness (AS) is also increased in these patients. AS is a recognised independent cardiovascular risk factor in adults [4].

Arterial stiffness has been commonly assessed using the SphygmoCor device to measure the pulse wave velocity (PWV) and we have previously used this methodology to study a group of children following heart transplantation and found a significantly increased PWV when compared with normal children [3]. However, this device is relatively expensive and we also found that there was a learning curve in using the equipment and it was intrusive at the femoral site.

A possible alternative technology is represented by photoplethysmography (PPG) [5], which is low-cost, easy-to-perform, and non-invasive. PPG uses an LED to shine a light beam through the human tissues and which is attenuated mainly by the blood cells according to the Beer-Lambert law (Equation 1); where I is the intensity of the beam after travelling a distance l, I_0 is its intensity at $l = 0$, α is the absorption coefficient, and c is the concentration of the absorbing material.

$$I = I_0 \exp(-\alpha l c) \quad (1)$$

A photodetector placed in a transmission or reflection mode then collects the attenuated light beam. This allows for the measurement of a microvascular peripheral pulse at different body sites, with the most commonly used being the ear, finger, and toe pad sites.

PPG has already shown value for different clinical applications in adults [6], including the assessment of cardiovascular ageing [7, 8, 9, 10].

The aim of this study was to assess photoplethysmographic pulse transit times at three different body sites in HTR in comparison to healthy children, and to explore their correlation with subject age and height.

2. Methods

2.1. Subjects

This study had ethical approval from a local Research Ethics Committee and all subjects provided written informed consent to participate from their parent or guardian.

Study groups included 12 HTR and 30 healthy children. The paediatric transplant recipients were recruited from the heart transplant clinic at the Freeman Hospital, Newcastle upon Tyne, UK. Patients were excluded if they were less than 6 years of age, they were less than 6 months after the transplantation, had a pacemaker, or had cardiac arrhythmias.

Healthy controls were recruited from local primary, middle, and secondary school in low to medium socio-economic communities of North Tyneside, UK. Controls were excluded from the study if they were on any medication except salbutamol, if they had a body mass index greater than 30 kg/m^2, smoked cigarettes, or had had caffeine less than 3 hours before their study commenced.

2.2. Pulse measurements

Signals were acquired using a PPG system operating in the infrared region (central wavelength 950 nm, bandwidth 50 nm) and working in reflection mode. PPG signals were recorded simultaneously from the right and left ear lobes, index fingers, and great toes for a duration of 150 s. The probes were kept firmly and comfortably in place with clips (ears) and Artema black Velcro cuffs (fingers and toes). A diagnostic bandwidth (0.05-100 Hz) ECG was also simultaneously recorded to provide a cardiac timing reference. The gain of dedicated amplifiers with a bandwidth of 0.5-20 Hz was adjusted for each PPG measurement, and separately for each channel, in order to maximise the dynamic range of the PPG signals. The ECG and PPG waveforms were digitised and stored to a computer at a sample rate of 2 kHz for subsequent analysis (Figure 1).

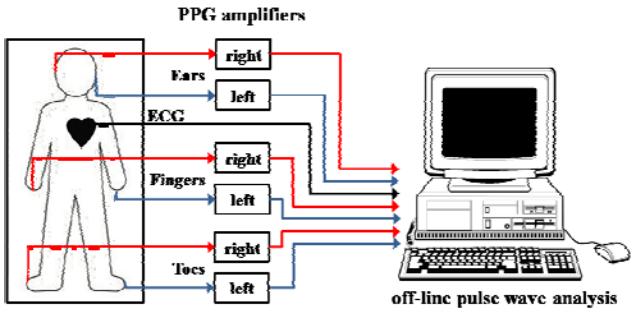

Figure 1. PPG measurement system.

2.3. Data and statistical analysis

Data were analysed off-line using bespoke pulse wave analysis software developed with Matlab.

The pulse transit time was defined as the time interval between the ECG R-peak and the PPG-pulse foot (Figure 2). For each subject, the median PTTf over a period of 60 heart beats was considered.

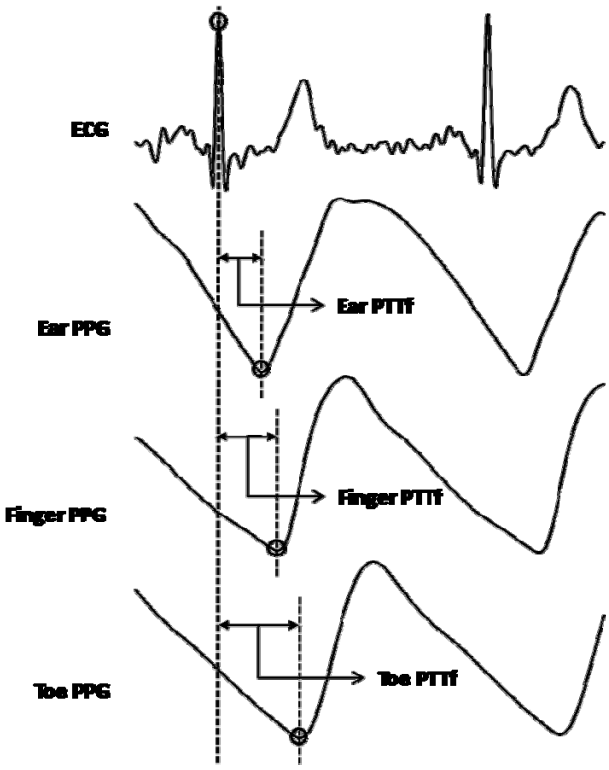

Figure 2. Definition of PPG pulse transit time measures: (1) Ear PTTf, (2) Finger PTTf, (3) Toe PTTf.

Values were summarised using non-parametric descriptive statistics in terms of median (lower quartile, Q1 – upper quartile, Q3). Similarity in PTTf values acquired from the left and right body sites were evaluated using the non-parametric Wilcoxon test. Differences between groups were assessed using the non-parametric Mann-Whitney *U*-test (for individual values) or the Fisher's exact test (for ratios). Possible linear regression between the PTTf measures and subject age and height were investigated with Spearman's correlation analysis. A *p*-value lower than 0.05 was considered to be statistically significant.

3. Results

The age range was 8 to 17 years for the HTR group, and 8 to 16 for the control group. The two study groups were not statistically different for gender distribution, age, and height (Table 1).

Table 1. Demographic data of the two groups.

n or median (Q_1-Q_3)	*HTR*	*Control*	*p-value*
Females / Males	7 / 5	15 / 15	0.7*
Age [years]	13.7 (8.8-16.2)	12.3 (9.0-14.9)	0.4**
Height [m]	1.53 (1.25-1.64)	1.53 (1.33-1.63)	0.9**

*from Fisher's exact test.
**from Mann-Whitney test.

3.1. Analysis of PTTf measures

The median right to left differences for the pulse transit time measures were 1.1 ms at the ears, 0.5 ms at the fingers, and -0.8 ms at the toes. These differences were not statistically significant [11]. Therefore, values from the right and left side were averaged at each body site for subsequent analysis.

Toe PTTf was significantly lower in HTR, 290 (275-302) ms, than in controls, 324 (296-336) ms, $p < 0.05$. No significant differences were found for the ear and finger PTTf measurements (Figure 3).

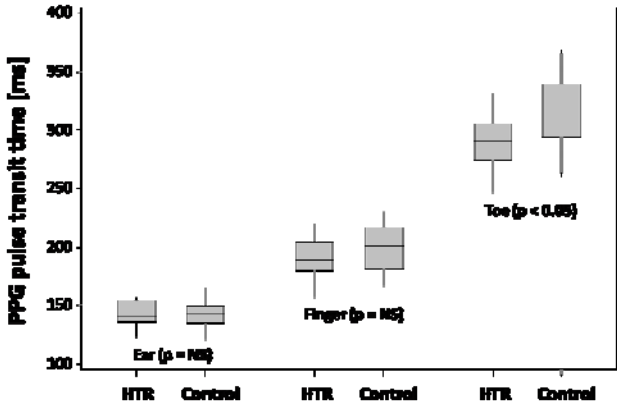

Figure 3. PPG pulse transit times for the HTR and control groups. Boxes represent the median, lower (Q_1), and upper (Q_3) quartiles; the whiskers go to the maximum and minimum value.

3.2. Correlation analysis

Results from correlation analysis of the PPG pulse transit time measures are reported in Table 2a (with subject age) and Table 2b (with subject height).

Toe PTTf significantly correlated with subject height both for the HTR and the control group (Figure 4). Equations derived from linear regression analysis, with height expressed in meters, were:

$$\text{HTR:} \quad \text{Toe PTTf [ms]} = 160 + 88 \cdot \text{height} \qquad (2.a)$$

$$\text{Control:} \quad \text{Toe PTTf [ms]} = 120 + 132 \cdot \text{height} \qquad (2.b)$$

Table 2a. Correlation of PTTf measures with subject age.

		ρ	*p-value*	*slope [ms/year]*
Ear PTTf	*HTR*	0.62	0.03	1.6
	Control	0.28	NS	n/a
Finger PTTf	*HTR*	0.52	NS	n/a
	Control	0.55	0.002	4.2
Toe PTTf	*HTR*	0.48	NS	n/a
	Control	0.59	< 0.001	7.2

Slopes of regression lines are provided for the cases where the correlation was significant. NS not significant. n/a not applicable.

Table 2b. Correlation of PTTf measures with subject height.

		ρ	*p-value*	*slope [ms/m]*
Ear PTTf	*HTR*	0.43	NS	n/a
	Control	0.35	NS	n/a
Finger PTTf	*HTR*	0.49	NS	n/a
	Control	0.71	< 0.001	76
Toe PTTf	*HTR*	0.78	0.002	88
	Control	0.76	< 0.001	132

Slopes of regression lines are provided for the cases where the correlation was significant. NS not significant. n/a not applicable.

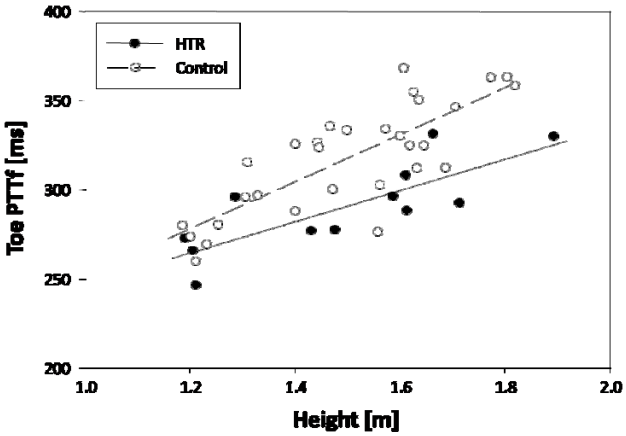

Figure 4. Regression lines between toe PTTf and height.

4. Discussion

This study has provided pilot data for the characterisation of the pulse transit time to three different body sites (ear, finger, and toe) in paediatric HTR and in comparison to healthy children.

In the presence of AS, the pulse wave travels faster through the arterial system and this leads to shorter PTTf

values. Therefore, the significantly shorter toe PTTf found in the HTR group is consistent with the expected AS. The median PTTf was also lower in HTR at the ear and finger, but this difference did not reach statistical significance at these sites. This finding agrees with other previous results [12, 13].

Correlation analysis showed that PTTf was significantly correlated with subject height in both groups only at the toe. The linear regression equation calculated for the HTR had a less steep slope than for controls (88 ms/m versus 132 ms/m). This is also consistent with the presence of AS in HTR, indicating that toe PTTf remained increasingly shorter in this group with increasing subject's height compared to controls. The loss of correlation in HTR at the finger with both age and height, and at the toe with age, may also be a consequence of cardiovascular disease. This aspect deserves further investigation in future studies.

Future studies should also investigate the correlation with other clinical variables, such as blood pressure parameters, heart rate, and body mass index. Differential PTTf between body sites could be considered in order to compensate for the inter-subject difference in the duration of the pre-ejection period [9]. Furthermore, body segmental lengths could be measured and used for the computation of pulse wave velocity.

5. Conclusions

This pilot study has shown a shorter pulse transit time at the toe for the HTR patients and this is consistent with the increased arterial stiffness expected in this group. Results from linear regression analysis have further corroborated this finding.

The value of photoplethysmographic assessment in this group has also been demonstrated.

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