Model based analysis of the variation in Korotkoff sound onset time during exercise

INSTITUTE OF PHYSICS PUBLISHING PHYSIOLOGICAL MEASUREMENT

Physiol. Meas. **22** (2001) 433–445 www.iop.org/Journals/pm PII: S0967-3334(01)17056-5

Model based analysis of the variation in Korotkoff sound onset time during exercise

A Türkmen[1] **and Y Z İder**[2]

[1] Baskent University, Department of Biomedical Engineering, 06530 Ankara, Turkey
[2] Bilkent University, Department of Electrical and Electronics Engineering, 06533 Ankara, Turkey

E-mail: turmen@baskent.edu.tr and ider@ee.bilkent.edu.tr

Received 11 September 2000, in final form 23 March 2001

Abstract

In this study, a minimal mathematical model of the cardiovascular system is used to study the effects of changes in arterial compliance and cardiac contractility on the onset time of Korotkoff sounds during an auscultatory procedure. The model provides blood pressure waveforms in the ventricle, the aorta and the brachial artery. From these waveforms, pre-ejection time, pulse propagation time and rise time of the blood pressure at the brachial artery can be computed. The time delay between onset time of ECG Q wave and onset time of Korotkoff sound is the sum of these three times. Rise time is zero and the time delay is minimal when the cuff pressure is slightly above the diastolic pressure. This minimum time delay is represented by QKD. Simulation results suggest that during the Bruce exercise protocol QKD decreases to one-third of its pre-exercise value if the cardiac contractility increases threefold. The effect of arterial compliance is not as significant as that of the cardiac contractility. From data recorded during an exercise test, it is observed that QKD decreases considerably as the test load is increased. We show in this study that the amount of decrease in QKD can be used as an index of the amount of increase in cardiac contractility during an exercise ECG test. Use of signal averaging for reducing the effect of motion artifacts during an exercise test is also shown to be very instrumental for making accurate QKD measurements.

Keywords: cardiovascular system modelling, Korotkoff sound, systolic pressure, diastolic pressure, cardiac contractility, arterial compliance, exercise test, pulse pressure propagation, pre-ejection time, QKD

1. Introduction

Cardiovascular disease is still one of the major sources of death in almost all countries (Kannel 1996), and, therefore, the need for developing new noninvasive diagnostic and monitoring methods for assessment of cardiovascular health persists. For this purpose, mathematical

models and computer simulations are being extensively used as information processing technology advances (Guarini *et al* 1998).

Korotkoff sounds have traditionally been used to measure systolic and diastolic arterial blood pressures noninvasively, employing the so-called auscultatory method. Other uses of Korotkoff sounds have also been proposed. Methods were derived which aim at assessing the level of distensibility of the arteries by relating the arterial compliance to the onset time of the Korotkoff sounds with respect to the ECG Q wave (Gosse *et al* 1994). Some investigators have attempted to construct the rising part of arterial pressure waveform by utilizing the variation of the onset time of the Korotkoff sounds recorded during noninvasive blood pressure measurement (Arzbaecher and Novotney 1973, Sharir *et al* 1993). However, the relation between timing of Korotkoff sounds and cardiovascular parameters has not been studied using a mathematical model. One aim of this study is to understand the effects of cardiovascular parameters on the timing of Korotkoff sounds using a minimal mathematical model.

The onset time of the ECG Q wave represents the beginning of left ventricular contraction. The time delay between onset time of the ECG Q wave and the onset time of the following Korotkoff sound is used as the measure of timing of Korotkoff sounds. This time delay, Q–K, is equal to the sum of three time intervals.

(i) *Pre-ejection time*. The time delay between the onset time of ECG Q wave and the opening of the aortic valve.
(ii) *Propagation time*. Propagation time of the pressure pulse from the heart (left ventricle) to the brachial artery.
(iii) *Rise time*. The time required for the arterial pressure to increase from the diastolic level to the level of the cuff pressure.

When the cuff pressure is adjusted to be slightly above the diastolic pressure, the rise time is zero and the time delay is minimal. This minimum time delay is represented by 'QKD'. In other words, QKD is equal to the sum of pre-ejection time and the propagation time. Effects of changes in two parameters, namely arterial compliance and cardiac contractility, on QKD are of main interest in this study. These two parameters can be used by clinicians in assessment of the state of a patient's cardiovascular system. Therefore, the inverse problem, that is, estimating these parameters from the measurements made on the Korotkoff sounds, can be of significant clinical importance.

Exercise ECG testing is widely used for cardiovascular diagnosis. Incorporation of QKD measurement to exercise ECG testing may be of additional clinical use, if it is demonstrated that QKD can be used for obtaining extra information about some cardiovascular parameters. In this study, ECG and Korotkoff sounds are simultaneously recorded during a treadmill exercise test. The data recorded during the test are post-processed to calculate the variation of QKD as exercise progresses. The results are discussed in light of the conclusions drawn from modeling and simulation studies.

2. Methods

2.1. Construction of a minimal mathematical model of the cardiovascular system

In order to investigate the timing of Korotkoff sounds, a model that incorporates the heart and the arterial system is needed. The model must be minimal, i.e., not more complex than it is necessary. Models using the varying-elastance model for the heart and a windkessel model for the arterial system have been used by several investigators (Stergiopulos *et al* 1996, Guarini *et al* 1998). The model proposed by Guarini *et al* differentiates between proximal and distal

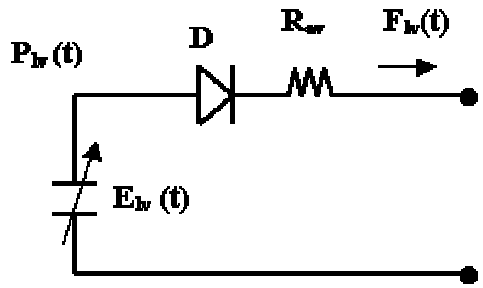

Figure 1. Left ventricle model.

parts of the aorta, and therefore we have based our studies on a similar model, because the pressure in the brachial artery when it is blocked by high cuff pressure is representative of the pressure in the distal part of the aorta.

The model is composed of two parts: the left ventricle model and the arterial load model. The left ventricle model is shown in figure 1. The left ventricle is modelled as a time varying elastance. The aortic valve is represented by an ideal diode and a resistor connected in series.

The elastance function $E_{\mathrm{lv}}(t)$ can be expressed as one of several analytical expressions such as a trapezoidal function, a sinusoidal function, a Gaussian function or a modified exponential function (Guarini *et al* 1998). A trapezoidal function is used as the elastance function in this study, because with this function the rise time of the elastance and its maximum value can be separately specified. The trapezoidal function is defined as follows:

$$E_{\mathrm{lv}}(t) = [0.99h(t) + 0.01] \tag{1}$$

where

$$h(t) = \begin{cases} (2.5/\mathrm{TS})^{*}t & \text{if } 0 < t < 0.4\ \mathrm{TS} \\ 1 & \text{if } 0.4\ \mathrm{TS} < t < 0.9\ \mathrm{TS} \\ (1 - (10^{*}t - 9\mathrm{TS})/\mathrm{TS}) & \text{if } 0.9\ \mathrm{TS} < t < \mathrm{TS} \\ 0 & \text{if } \mathrm{TS} < t < \mathrm{TH} \end{cases} \tag{2}$$

where TS is systole duration, TH is total heart beat period and $E_{\max}$ is the maximum elastance value reached in a cardiac cycle.

The minimum elastance is assumed to be 1% of the maximum elastance value. Values of TS, TH and $E_{\max}$ specify the left heart elastance function completely. A graph of $E_{\mathrm{lv}}(t)$ is shown in figure 2 for TS = 0.4 s, TH = 1 s and $E_{\max} = 2$ mm Hg ml^{-1}.

The arterial load is composed of lumped elements as shown in figure 3. C_{ap} and C_{ad} represent the proximal and distal arterial compliances respectively, and L represents the blood mass inertia. The inclusion of two compliances and an inertance is in line with previous studies (Guarini *et al* 1998, Goldwyn and Watt 1967). R_{sc} is the systemic peripheral resistance and $P_{\min}$ is the venous pressure. The flow $F_{\mathrm{lv}}(t)$ is the flow supplied from the left ventricle. $P_{\mathrm{ap}}(t)$ is the proximal pressure of the aorta and $P_{\mathrm{ad}}(t)$ is the distal pressure, which is equivalent to the brachial artery pressure.

Left ventricle pressure at any time is equal to the product of the volume and elastance of the left ventricle. The diode in the left ventricle is ON when the left ventricle pressure is higher than $P_{\mathrm{ap}}(t)$. Differential equations which are derived from the model are solved by numerical integration using the trapezoidal method. The integration step is chosen as 0.0001 s.

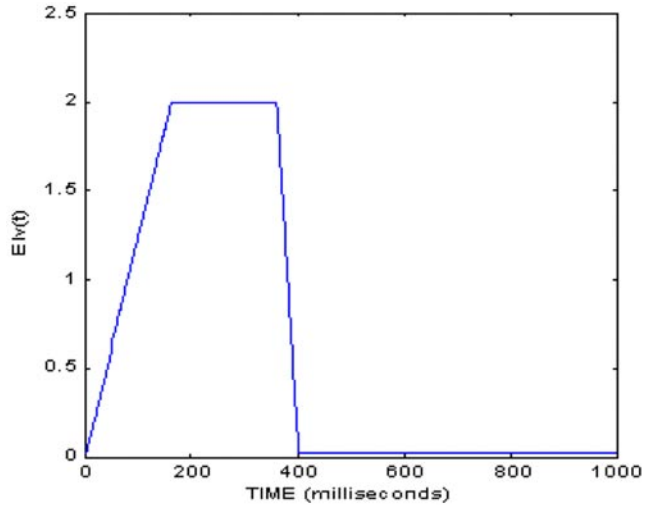

Figure 2. Left ventricular elastance function $E_{\mathrm{lv}}(t)$ = for TH = 1 s, TS = 0.4 s and $E_{\max} = 2$ mm Hg ml^{-1}.

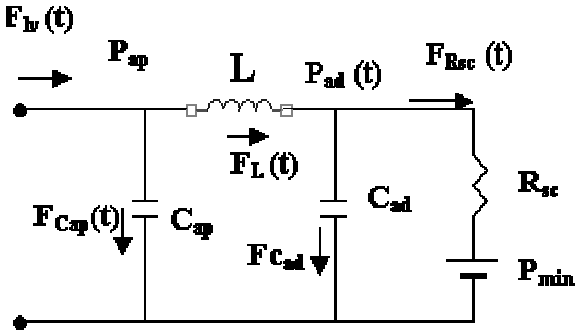

Figure 3. The arterial load model.

Table 1. Slope, speed and duration of each step of exercise test according to the Bruce protocol.

Step	Slope (%)	Speed (km h^{-1})	Time (min)
1	10	2.8	3
2	12	4.1	3
3	14	5.4	3
4	16	6.8	3
5	18	8.0	3
6	20	8.8	3
7	22	9.6	3

2.2. QKD measurement during exercise test

The Bruce protocol is used in this study during a treadmill stress test. Slope, speed and durations of each step of the Bruce protocol are given in table 1. A data acquisition system

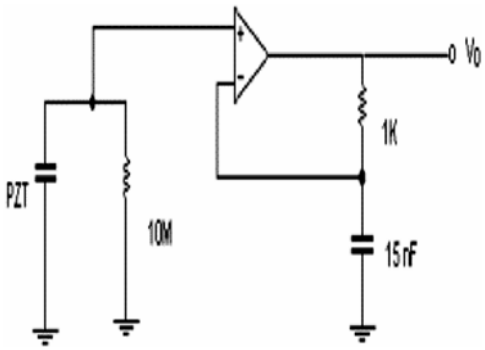

Figure 4. Piezoelectric transducer and charge amplifier.

Table 2. Parameter values used in the sample study.

Parameter	Value	Unit
R_{av}	0.025	mm Hg s ml^{-1}
R_{sc}	0.85	mm Hg s ml^{-1}
C_{ad}	0.06	ml (mm Hg)$^{-1}$
C_{ap}	1.8	ml (mm Hg)$^{-1}$
E_{max}	2.0	mm Hg ml^{-1}
$V_{lv}(0)$	130	ml
P_{min}	30	mm Hg
L	0.012	mm Hg s^2 ml^{-1}
TS	0.4	s
TH	1.0	s

is developed to record ECG, Korotkoff sounds and cuff pressure simultaneously during 20 s of rest and the whole period of exercise test. A sampling rate of 500 samples s^{-1} is used. Details of the data acquisition are explained in the thesis of Turkmen (2000). Korotkoff sound recording is based on a charge amplifier using a piezoelectric transducer, as shown in figure 4. The piezoelectric transducer is placed over the brachial artery near the elbow, the standard location where a stethoscope is placed by physicians to hear Korotkoff sounds.

3. Results

3.1. Pressure waveforms

Simulations are made using the model to obtain waveforms of the pressures in the ventricle, in the proximal aorta and in the brachial artery during a complete heart cycle. Numerical integration is continued until several heart cycles elapse and steady state is reached. Parameter values used in this sample study are taken from Guarini *et al* (1998). They have used parameter identification techniques to estimate these parameters as applied to real data taken from a large population of subjects, and they have reported ranges for the parameters. We have used approximately the midpoints of the parameter ranges reported by Guarini *et al* (1998). These values are listed in table 2 and the corresponding computed pressure waveforms are shown in figures 5 and 6.

The filling phase of the left ventricle is not simulated in this study because waveforms of pressure and volume in the left ventricle during filling do not affect brachial artery pressure

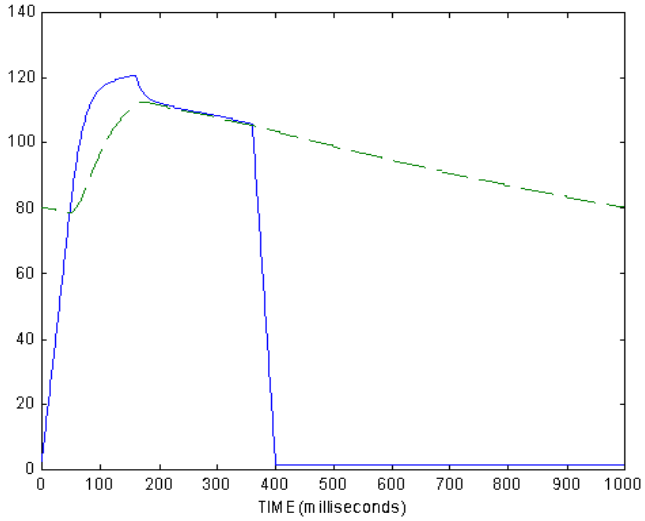

Figure 5. Pressure waveforms, $P_{\mathrm{lv}}(t)$ (solid curve) and $P_{\mathrm{ap}}(t)$ (dashed curve).

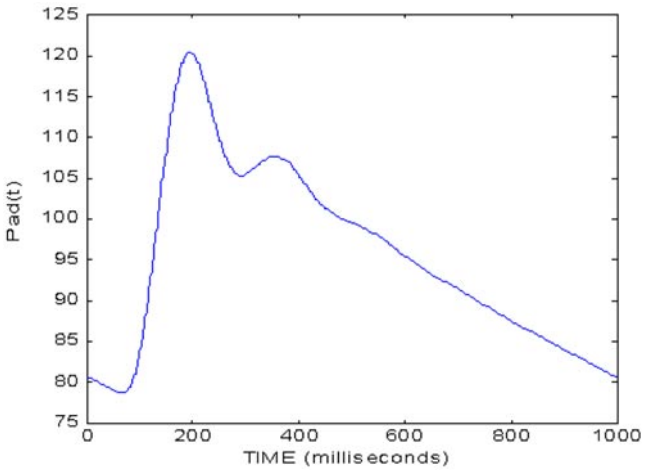

Figure 6. The brachial artery pressure waveform.

waveform, the main variable of interest in this study. At the beginning of each contraction, left ventricle volume is taken to be 130 ml. Computations are made for a duration of several heartbeats, and hence, steady state pressure–flow-volume values and waveforms are obtained (Guarini *et al* 1998).

Initially, left ventricle pressure is 1.06 mm Hg, and it increases from this value as contraction begins. Left ventricular pressure is proportional to the value of the elastance function until the aortic valve opens. Left ventricular pressure exceeds the pressure in the aorta and hence the aortic valve opens at $t = 49$ ms. From then on, blood volume inside the left ventricle decreases since blood flows through the aortic valve out from the left ventricle. The aortic valve remains open until it closes at $t = 367$ ms.

When ventricular contraction begins, brachial artery pressure is 80.65 mm Hg and pressure in the proximal aorta is 80.2 mm Hg. Both of these pressures are still decreasing when the

Table 3. Sensitivities of model variables to model parameters.

	Variables				
Parameters	Diastolic pressure	Systolic pressure	QKD	Pre-ejection time	Propagation time
E_{max}	+0.28	+0.33	−0.56	−0.76	0
C_{ap}	+0.2	−0.14	+0.19	+0.21	+0.12
C_{ad}	+0.004	+0.07	+0.09	−0.042	+0.46
R_{sc}	+0.62	+0.4	+0.46	+0.59	+0.12

ventricular contraction begins. Pressure in the proximal aorta begins to increase when the aortic valve opens at $t = 49$ ms. Brachial artery pressure starts to increase after the pulse pressure propagates and reaches the brachial artery. In this sample study, brachial artery pressure continues to decrease until it reaches its minimum value at $t = 68$ ms. Minimum value of the brachial artery pressure, i.e. diastolic pressure, is 78.7 mm Hg. Brachial artery pressure starts to increase afterwards. It reaches the maximum value at $t = 171$ ms. The maximum value, i.e. systolic pressure, is equal to 120.8 mm Hg.

The maximum value of Q–K is 171 ms and it is obtained when the cuff pressure is equal to the systolic pressure. Q–K becomes minimum when the cuff pressure is equal to the diastolic pressure. The minimum value of Q–K, represented by QKD, for this sample study is 68 ms. At $t =$ QKD, decrease in the brachial artery pressure comes to an end and it begins to increase. Pre-ejection time, i.e., the time delay between beginning of ventricular contraction and opening of the aortic valve, is 49 ms. Propagation time of the pressure pulse from the aortic valve to the brachial artery, or the Korotkoff sound generation site, is equal to the difference between QKD and the pre-ejection time. Propagation time is 68–49 = 19 ms in this sample simulation.

3.2. Sensitivity analysis

Sensitivity analysis is a useful tool for investigating the relative effects of model parameters to various outputs of a model (Stergiopulos *et al* 1996). To assess the relative sensitivities of QKD and its components to model parameters, sensitivity analysis is performed. Sensitivity of a variable Y to a parameter X is defined as

$$\text{sensitivity} = (\Delta Y/Y)/(\Delta X/X). \tag{3}$$

Sensitivities of QKD, pre-ejection time and propogation time to E_{max}, C_{ap}, C_{ad} and R_{sc} are calculated around the operating point defined by the model parameters given in table 2. The results are given in table 3. As seen in table 3, QKD has a high negative sensitivity to E_{max}. All of this sensitivity is due to the sensitivity of pre-ejection time to E_{max}, the sensitivity of propagation time to E_{max} being zero. QKD has high sensitivity to C_{ap} and R_{sc}. These effects are also mostly due to the sensitivity of pre-ejection time to C_{ap} and R_{sc}.

In table 3, sensitivities of diastolic and systolic pressures to model parameters are also listed. It is observed that accompanying a negative sensitivity of QKD to E_{max}, there is a positive sensitivity of diastolic pressure to this parameter. However, an increase in diastolic pressure directly influences pre-ejection time and consequently QKD, because the time it takes for ventricular pressure to reach the value of diastolic pressure increases. Thus, in general, the sensitivities shown in table 3 include the additional effects of changes in diastolic pressure. In order to quantitate the sensitivity of a variable to model parameters, independent of the effects of changing diastolic pressure, a modified sensitivity analysis is performed.

Table 4. Modified sensitivities of model variables to model parameters.

	Variables		
Parameters	QKD	Pre-ejection time	Propagation time
E_{max}	−0.77	−1.01	−0.12
C_{ap}	+0.03	−0.04	+0.23
C_{ad}	+0.06	−0.04	+0.35

In the modified sensitivity analysis, when a parameter is perturbed, the peripheral resistance R_{sc} is also changed in the appropriate direction in order to keep diastolic pressure unchanged. It is known that during exercise testing, blood pressure is heavily regulated by the CNS through controlling R_{sc}. Therefore, the modified sensitivity analysis is more appropriate for the purposes of this study which focuses on observations during exercise.

Results of the modified sensitivity analysis are shown in table 4. It is observed that if diastolic pressure is kept constant, QKD is more sensitive to E_{max}, and most of this sensitivity is again accounted for by the sensitivity of pre-ejection time to E_{max}. On the other hand, C_{ap} and C_{ad} do not affect pre-ejection time but only propagation time. Overall, the most significant parameter that changes QKD is E_{max}.

3.3. Dependence of QKD on cardiac contractility and arterial compliance in their physiological ranges

The sensitivity analysis explained in the previous section is a small signal analysis tool, which is performed around the operating point. In this section, simulations are made to investigate the large-signal relations between cardiovascular parameters and QKD. The cardiovascular parameters of interest are cardiac contractility and arterial compliance. Values of cardiac contractility and arterial compliance are changed in their physiological limits while these simulations are made.

3.3.1. Effect of cardiac contractility on QKD. To see the effect of changing cardiac contractility on the brachial artery pressure waveform and the QKD, the simulation program is run with several different values of the maximum contractility, E_{max}. However, a rise in E_{max} increases the diastolic pressure, and this, in turn, causes an increase in QKD. Since we are interested in understanding the sole effect of E_{max} on QKD, R_{sc} is reduced to keep the diastolic pressure constant. Hence, the increase in QKD due to the rise in the diastolic pressure is eliminated. The difference in QKD computed after this correction is completely due to the change in E_{max}.

Results are listed in table 5. Variation of QKD and pre-ejection time with E_{max} is plotted in figure 7. As seen in the table, diastolic pressure is kept between 79.5 and 80.5 mm Hg. Systolic pressure, QKD and pre-ejection time are given in the table, too. The value of the systemic resistance R_{sc} for each case is also given. It is seen clearly from table 5 and figure 7 that QKD and the pre-ejection time strongly depend on cardiac contractility. Both QKD and pre-ejection time decrease considerably as E_{max} is increased. In this study, E_{max} is increased from 1.2 mm Hg ml^{-1} to 3.9 mm Hg ml^{-1}. With this increase in E_{max}, QKD decreases from 103 to 42 ms. Pre-ejection time decreases from 85 to 27 ms. Pulse propagation time decreases from 18 to 15 ms.

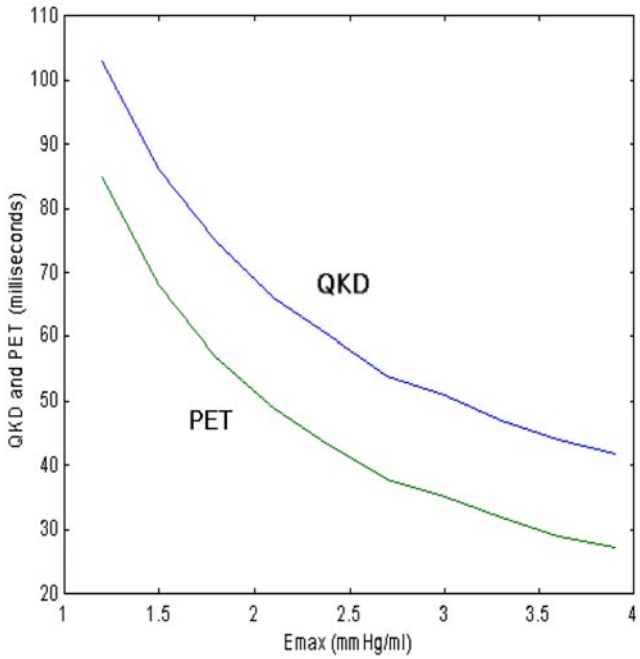

Figure 7. $E_{\max}$ (maximum cardiac contractility) against QKD and PET (pre-ejection time). $E_{\max}$ is in mm Hg ml^{-1}; QKD and PET are in milliseconds.

Table 5. Values of the diastolic and systolic pressures, QKD and pre-ejection time for several values of $E_{\max}$.

$E_{\max}$ (mm Hg ml^{-1})	P_d (mm Hg)	P_s (mm Hg)	QKD (milliseconds)	Pre-ejection time (milliseconds)	R_{sc} (mm Hg s ml^{-1})
1.2	79.92	109.90	103	85	1.2689
1.5	80.04	115.75	86	68	1.0367
1.8	80.15	119.82	75	57	0.9238
2.1	80.01	122.66	66	49	0.8532
2.4	79.82	124.84	60	43	0.8057
2.7	79.63	126.66	54	38	0.7720
3.0	80.04	128.81	51	35	0.7543
3.3	80.04	130.35	47	32	0.7365
3.6	80.05	131.74	44	29	0.7224
3.9	80.05	133.00	42	27	0.7110

3.3.2. Effect of arterial compliance on QKD. The two parameters in the model, C_{ap} and C_{ad}, represent the equivalent lumped compliances of the arterial load. To study the effect of a change in the arterial compliance, the simulation program is run with several different values of these two compliances. Diastolic pressure is kept at around 80 mm Hg (between 79.5 and 80.5) by changing the value of systemic resistance. Hence, the change in QKD due to the change in the diastolic pressure is eliminated again. The net change in QKD computed by this method is completely due to the change in arterial compliance. The computed QKD and pre-ejection time values are listed in table 6.

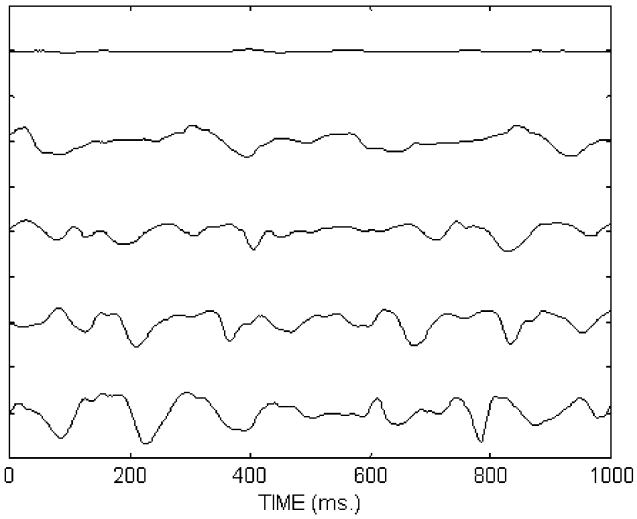

Figure 8. Motion artefacts recorded at resting and steps 1, 2, 3 and 4 of an exercise test. While these sounds were recorded the cuff pressure was above the systolic pressure. (Vertical units are arbitrary but the same for all waveforms.)

Table 6. Values of the diastolic and systolic pressures, QKD and pre-ejection time for several values of C_{ap} and C_{ad}.

C_{ap} ml (mm Hg)$^{-1}$	C_{ad} ml (mm Hg)$^{-1}$	QKD (milliseconds)	Pre-ejection time (milliseconds)
0.6	0.04	64	51
1.2	0.04	66	51
1.8	0.04	66	51
0.6	0.08	63	52
1.2	0.08	70	52
1.8	0.08	71	52
1.2	0.12	64	52
1.8	0.12	71	52

As shown in table 6, pre-ejection time remains constant while the compliance changes. QKD and the pulse propagation time increase as the values of the compliances (C_{ap} and C_{ad}) increase. QKD increases from 64 ms to 71 ms. The propagation time increases from 13 ms to 19 ms.

Simulation results show that values of both arterial compliance and cardiac contractility affect the value of QKD. Effect of a change in cardiac contractility on QKD is much higher than the effect of a change in the value of arterial compliance, within the physiological ranges of the elastance and compliance parameters.

3.4. Measurements during exercise ECG testing

The signals shown in figure 8 are the recorded sound signals when the cuff pressure was higher than the systolic pressure. Korotkoff sounds are not generated at these cuff pressures. Therefore, these signals are only motion artefacts. As it can be seen in these signals, amplitudes of the motion artefacts increase at each higher step of the test.

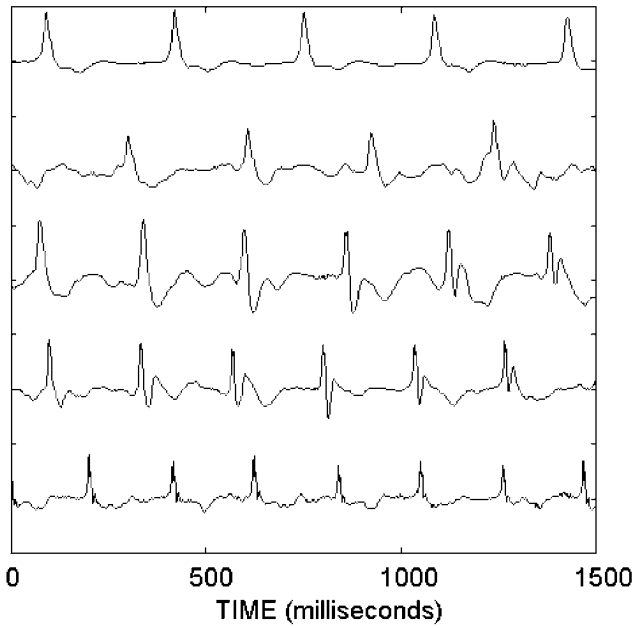

Figure 9. Korotkoff sounds and motion artefacts recorded at rest and steps 1, 2, 3 and 4 of an exercise test. The cuff pressure was between the systolic pressure and diastolic pressure when these sounds were recorded. (Vertical units are arbitrary but the same for all waveforms.)

The signals shown in figure 9 are the recorded signals at rest and at steps 1–4 of an exercise test. To observe the variation of QKD at each step of the test, the effects of the motion artefacts must be removed from the recorded sound signal (Au *et al* 1995). In other words, an accurate waveform of the Korotkoff sound recorded while the cuff pressure was equal to the diastolic pressure is needed. From this waveform, QKD can be computed. In this study, the cuff pressure was kept near the diastolic pressure for a duration of 10–15 heart periods. Hence, more than ten Korotkoff sounds were recorded. The Korotkoff sounds were aligned taking the onset of the ECG Q wave as reference, and then these sounds were averaged to reduce the motion artefacts.

The waveforms depicted in figure 10 are average Korotkoff sounds at rest and at steps 1–4 of an exercise test. The cuff pressure was close to the diastolic pressure when these sounds were recorded. The time $t = 0$ ms corresponds to the onset time of the ECG Q wave. Onsets of the Korotkoff sounds are visually determined. QKD is determined to be 145 ms at rest. At step 1 of the test, QKD becomes 130 ms. It decreases to 100 ms at step 2, to 90 ms at step 3 and to 70 ms at step 4. Similar decreases in QKD are observed in recordings of five subjects.

4. Discussion and conclusion

QKD is measured for the Korotkoff sounds recorded at several steps of the exercise test for a subject in this study. It is observed from our recordings that the heart rate increases and QKD decreases at each higher step of the exercise test. Diastolic pressure was approximately 70 mm Hg at rest. It increased by 10–30 mm Hg during the test. The diastolic pressure increased for other subjects as well approximately in this range. It is known from the simulation results that as the diastolic pressure increases, QKD increases. However, the recorded data

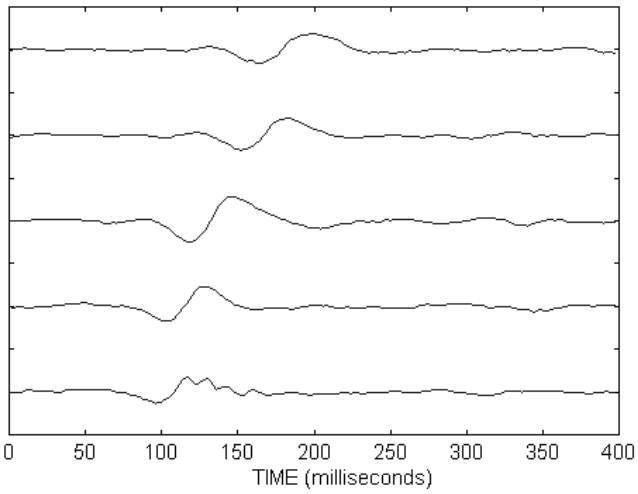

Figure 10. Average of last Korotkoff sounds recorded at rest and steps 1–4 of an exercise test. The vertical scale is arbitrary but the same for all waveforms.

and analysis results show clearly that QKD decreases as the exercise load is increased, i.e., speed and slope of the treadmill are increased.

As the subject performs heavier exercise, the body demands higher amounts of oxygen. The heart contracts more strongly to circulate more amount of blood and hence oxygen to the tissues. Hence, increase in cardiac contractility is expected naturally during an exercise test (Guyton 1996). However, compliance of the main arteries is not expected to change significantly during such a test (Guyton 1996). Therefore, it can be concluded that QKD decreases during the exercise test due to an increase in cardiac contractility. The model also supports this idea. Simulation results also show quantitatively that the significant decrease in QKD can only be related to an increase in cardiac contractility.

It can be concluded from this study that QKD considerably decreases during an exercise test due to an increase in cardiac contractility. It is therefore proposed that the decrease in QKD can be used as an index for the amount of increase in cardiac contractility during an exercise test. Incorporation of the methods developed in this study into stress ECG testing, and the use of Korotkoff sound derived indices with regard to the state of cardiovascular system of the patient may be very useful.

Measurement of QKD during an exercise test, on the other hand, requires special attention due to the noise introduced mainly by motion artefacts. In this study, this problem is handled by introducing the concept of signal averaging, by the use of which Korotkoff sounds with sufficient fidelity are obtained.

For the validation of the proposed method clinically, further studies must be undertaken. Drugs which are known to alter cardiac contractility may be employed. Similarly, measurement of $(\mathrm{d}P/\mathrm{d}t)$ via intraventricular pressure transducers can be utilized for direct verification of any change in cardiac contractility. Furthermore there is potential for using QKD for prognostic use for patients who are undergoing therapeutic procedures.

References

Arzbaecher R C and Novotney R L 1973 Noninvasive measurement of the arterial pressure contour in man *Bibl. Cardiol.* **31** 63

Au T C-pong, Webster J G and Tan B T 1995 A system for non-invasively measuring blood pressure on a treadmill *Physiol. Meas.* **16** 273–85

Goldwyn R M and Watt T B 1967 Arterial pressure pulse contour analysis via a mathematical model for the clinical quantification of human vascular properties *IEEE Trans. Biomed. Eng.* **14** 11–17

Gosse P, Guillo P, Ascher G and Clementy J 1994 Assessment of arterial distensibility by monitoring the timing of Korotkoff sounds *Am. J. Heart* **7** 228–33

Guarini M, Urzúa J, Cipriano A and González W 1998 Estimation of cardiac function from computer analysis of the arterial pressure waveform *IEEE Trans. Biomed. Eng.* **45** 1420–8

Guyton A C 1996 *Textbook of Medical Physiology* (Philadelphia, PA: Saunders)

Kannel W B 1996 Incidence, prevalence, and mortality of coronary artery disease *Atherosclerosis and Coronary Artery Disease* ed V Fuster, R Ross and E J Topol (Philadelphia, PA: Lippincott) pp 13–14

Sharir T *et al* 1993 Validation of a method for noninvasive measurement of central arterial pressure *Hypertension* **21** 74–82

Stergiopulos N, Meister J-J and Westerhof N 1996 Determinants of stroke volume systolic and diastolic aortic pressure *Am. J. Physiol.* **270** H2050–9

Turkmen A 2000 Development of methods for noninvasive assessment of the cardiovascular system using Korotkoff sounds *PhD Thesis* Middle East Technical University