Year : 2011

Enhanced diastolic reflections on arterial pressure pulse during exercise recovery

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THESE

préparée sous la direction du Professeur associé François Feihl

(avec la co-direction du Professeur Bernard Waeber)

et présentée à la Faculté de biologie et de médecine de
l'Université de Lausanne pour l'obtention du grade de

DOCTEUR EN MEDECINE

par

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Médecin diplômé de la Confédération Suisse
Originaire de Höri (Zürich)

Lausanne
2011

UNIL | Université de Lausanne
Faculté de biologie et de médecine

Ecole Doctorale
Doctorat en médecine

Imprimatur

Vu le rapport présenté par le jury d'examen, composé de

Directeur de thèse	*Monsieur le Professeur associé* ***François Feihl***
Co-Directeur de thèse	*Monsieur le Professeur* ***Bernard Waeber***
Expert	
Directrice de l'Ecole doctorale	*Madame le Professeur* ***Stephanie Clarke***

la Commission MD de l'Ecole doctorale autorise l'impression de la thèse de

Monsieur Benoît Dischl

intitulée

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Lausanne, le 7 juillet 2011

pour Le Doyen
de la Faculté de Biologie et de Médecine

Madame le Professeur Stephanie Clarke
Directrice de l'Ecole doctorale

REMERCIEMENTS

Je tiens à remercier particulièrement le Professeur François Feihl sans lequel ce travail n'aurait tout simplement pas pu voir le jour. Son enthousiasme et ses qualités scientifiques hors normes, avec en particulier plusieurs idées originales d'interprétation des résultats, ont été décisifs dans l'aboutissement du projet.

Je remercie également le Professeur Bernard Waeber pour son soutien. Grâce à son entregent, une collaboration scientifique a une nouvelle fois été possible avec un service extérieur à la Division de Physiopathologie clinique.

Enfin, je remercie Madame Françoise Bilat, secrétaire de la Division de Physiopathologie clinique, pour sa grande disponibilité et son important soutien logistique.

RESUME

Durant la phase de récupération d'un exercice de course à pied d'intensité maximale ou submaximale, une augmentation de la pression artérielle systolique centrale (aortique) résultant de la réflexion des ondes de pouls sur l'arbre vasculaire est constatée chez l'individu en bonne santé. En diastole cependant, l'impact de la réflexion de ces ondes de pouls sur la pression centrale demeure inconnu durant la récupération d'un exercice.

Nous avons évalué les ondes de pouls centrales systolique et diastolique chez onze athlètes d'endurance durant la phase de récupération d'un exercice de course à pied dans des conditions d'effort maximal (sur tapis de course) et lors d'un effort submaximal lors d'une course à pied de 4000 mètres en plein air sur terrain mixte.

Pour chaque sujet et lors des deux exercices, l'onde de pouls a été mesurée au niveau radial par tonométrie d'aplanation durant une phase de repos précédant l'exercice, puis à 5, 15, 25, 35 et 45 minutes après la fin de l'exercice. En utilisant une fonction mathématique de transfert, l'onde de pouls centrale a été extrapolée à partir de l'onde de pouls radiale. En compilant la forme de l'onde de pouls centrale avec une mesure simultanée de la pression artérielle brachiale, un index d'augmentation de l'onde de pouls en systole (AIx) et en diastole (AIs) peut être calculé, reflétant l'augmentation des pressions résultant de la réflexion des ondes sur l'arbre vasculaire périphérique.

A 5 minutes de la fin de l'exercice, les deux index ont été mesurés moindres que ceux mesurés lors de la phase précédant celui-ci. Lors des mesures suivantes, AIx est resté bas, alors que AId a progressivement augmenté pour finalement dépasser la valeur de repos après 45 minutes de récupération. Le même phénomène a été constaté pour les deux modalités d'exercice (maximal ou submaximal). Ainsi, au-delà de quelques minutes de récupération après un exercice de course d'intensité maximale ou submaximale, nous avons montré par ces investigations que les ondes de pouls réfléchies en périphérie augmentent de façon sélective la pression centrale en diastole chez l'athlète d'endurance.

ENHANCED DIASTOLIC REFLECTIONS ON ARTERIAL PRESSURE PULSE DURING EXERCISE RECOVERY

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Accepted for publication in Scandinavian Journal of Medicine and Science in Sports, 2011

ABSTRACT

During recovery from a maximal or submaximal aerobic exercise, augmentation of central (aortic) systolic pressure by reflected pressure waves is blunted in healthy humans. However, the extent to which reflected pressure waves modify the central pulse in diastole in these conditions remains unknown. We evaluated systolic and diastolic central reflected waves in 11 endurance-trained athletes on recovery from a maximal running test on a treadmill (treadmill-max) and a 4000m run in field conditions. On both occasions in each subject, the radial pulse was recorded with applanation tonometry in the resting preexercise state and then 5, 15, 25, 35, and 45 minutes after exercise termination. From the central waveform, as reconstructed by application of a generalized transfer function, we computed a systolic (AIx) and a diastolic index (AId) of pressure augmentation by reflections. At 5 minutes, both indices were below preexercise. At further time-points, AIx remained low, while AId progressively increased, to overshoot above preexercise at 45 minutes. The same behavior was observed with both exercise types. Beyond the first few minutes of recovery following either maximal or submaximal aerobic exercise, reflected waves selectively augment the central pressure pulse in diastole, at least in endurance-trained athletes.

INTRODUCTION

In the course of physical activity, the increased metabolic needs of the body are met by an increase of cardiac output above its resting level, associated with a drop in systemic vascular resistance (SVR), the latter largely reflecting vasodilation of resistance vessels (small arteries and arterioles) in exercising skeletal muscle. At least with strenuous effort, the balance of cardiac output and SVR changes is such that blood pressure rises [1]. On return to the resting state, this physiological response progressively abates, but SVR may remain low for an extended period (several hours) [2], sometimes leading to post-exercise hypotension [3]. Exercise-induced relaxation of vascular smooth muscle is not limited to resistance vessels, but concerns conduit arteries as well, and this may also last well into the post-exercise recovery period [4,5]. Such persistent relaxation probably explains the post-exercise increase in arterial distensibility, which appears more marked in muscular than in elastic large arteries [4].

The pressure in the central (ascending) part of the aorta has especial physiological relevance, because in systole it is an essential determinant of left ventricular afterload, and in diastole it represents the driving force of myocardial perfusion. The shape of the central aortic pressure waveform (central pulse contour) results from complex interactions between the pattern of left ventricular ejection, the elastic behavior of conduit arteries, the SVR, and the multiple wave reflections which occur at sites of impedance mismatch scattered throughout the arterial tree [6]. Reflected pressure waves travel backwards towards the heart, superimposing on the forward wave generated by ventricular contraction, thus modifying the shape of the arterial pressure pulse to an extent dependent on both their amplitude and timing. Reflection amplitude is determined by the degree of impedance mismatch at the reflection sites, while timing depends on the traveling velocity of pressure waves along the arterial

tree (pulse wave velocity, PWV) and the length of the travel path. PWV is inversely related to vessel distensibility through the Moens-Korteweg equation [6]. Thus, in the ascending aorta where travel path to and from the reflection site is maximal, and with compliant arteries making up for low PWV, a large part of reflections is expected in diastole, and this is indeed what happens in young healthy adults [7]. With stiffer arteries by contrast, as occurs with advancing age or presence of cardiovascular risk factors, reflected waves may substantially augment peak aortic pressure in systole [6,7,8,9].

The pattern of aortic pressure modification by reflected waves in the course of recovery from acute exercise has been incompletely characterized. Based on the aforementioned changes in arterial distensibility, one would expect augmentation of central systolic pressure to become less prominent, or even entirely abolished, and this has indeed been observed in young healthy subjects, following exercise to either maximal [10] or submaximal aerobic capacity [11]. These studies were focused on systolic events. It remains unknown whether the augmentation of diastolic aortic pressure by reflected waves is also modified in the course of recovery from aerobic exercise. In theory, such modification could consist in diastolic augmentation becoming more marked, due to a shift of reflection timing away from systole and towards diastole. Alternatively, aortic pressure augmentation could be blunted in all parts of the cardiac cycle, because vasodilation would attenuate impedance mismatch at reflection-generating sites. Clearing up this point is not only of academic interest, because it impacts on the determinants of post-exercise coronary perfusion pressure. Indeed, myocardial ischemia sometimes occurs in the recovery period following exercise testing for coronary artery disease [12].

The present study was carried out in endurance-trained young athletes. In these subjects, we reconstructed the central aortic pressure waveform from the

noninvasive recording of radial pulse with applanation tonometry, repeatedly carried out in the first 45 minutes of rest following either a treadmill test to full aerobic capacity, or a 4000 meter run.

METHODS

Subjects

Eleven competitive endurance-trained male athletes aged between 20 and 40 years were recruited at the Swiss Olympic Medical Center, Lausanne, Switzerland. All subjects were healthy, with an inconspicuous medical history, and none was currently on any medication. All had had a weekly aerobic activity of at least two hours during the last twelve weeks. Their mean demographic data (± SD) were: age 33 ± 5 years, weight 73.1 ± 6.9 kg, height 181±4 cm, body mass index 22.2 ± 1.8 kg/m^2). Their mean maximal oxygen consumption (VO2max), measured as described below, was 62 ± 5 mL/kg/min.

All subjects gave their written consent to participate to this study after been fully informed on the study protocol. The investigation conformed with the principles outlined in the declaration of Helsinki and was approved by the Ethical Commission of our hospital.

Measurements

Brachial blood pressure was obtained with a mercury sphygmomanometer (Mercuro 300, Riester; Germany) by averaging the last two of 3 readings. Applanation tonometry of the radial artery was carried out in triplicate, using the Sphygmocor device (AtCor Medical, Sydney, Australia) as previously described by our group [13,14]. 10 seconds recordings were accumulated until three were available that fulfilled all quality criteria defined by the manufacturer, i.e. a mean pulsatile amplitude of the raw tonometric signal higher than 80 mV, as well as a beat-to-beat variability of pulse pressure and of diastolic pressure < 5% of average pulse pressure. Recordings not fulfilling these criteria were discarded. Sphygmomanometry and applanation

tonometry were carried out by the same investigator, with subjects in the semi-recumbent position with the thorax tilted at 30° above horizontal and forearms supported by armrests.

VO_2max was assessed using the CPX/MAX system (MedGraphics, St. Paul, MN 55127, U.S.A).

Protocol

Each participant was examined on two sessions taking place a minimum of three and a maximum of 15 days apart. Sphygmomanometry and radial applanation tonometry were carried out at rest (baseline). Then, subjects warmed-up for 15 minutes before carrying out either a maximal intensity running test on a treadmill on one session (*treadmill-max*), or a 4000 meters run carried out at submaximal speed on a another session (*4000m-submax*). The 4000 meter run was part of the subjects regular training program. Sphygmomanometry and radial applanation tonometry were carried out again 5, 15, 25, 35, and 45 minutes after exercise termination.

The order of application of the two exercise types was randomized. VO2max was measured in the course of the maximal intensity running test, which conformed to a Wasserman graded protocol and took place in the exercise physiology laboratory. All 4000m runs took place outdoors, on the same track, , at a pace of 4.5 minutes per kilometer, as given by the same instructor throughout the study.

Data analysis

The central aortic pressure waveform was reconstructed from the radial pulse, using the generalized transfer function method as implemented in the Sphygmocor device, and abundantly described elsewhere [15,16].

To obtain a graphical overview of the influence of experimental conditions on the radial and central arterial pulse waveforms, these were ensemble-averaged and expressed in percent of the corresponding pulse pressure as previously described [13,14].

From the radial pressure waveform, the Sphygmocor software estimates ejection duration as the time from the foot of the pressure wave to the incisura. On both the radial and reconstructed central pressure waveforms, it then positions the systolic points P1 (the peak of the forward pressure wave) and P2 (the peak of the reflected systolic wave) as shown on Figure 1. The time lag separating P2 from P1 (ΔT) gives an estimate of twice the travel time of the systolic reflected wave. The relative importance of the forward and reflected pressure waves is expressed as a systolic augmentation index AI according to the formula:

$$AI = 100 \times (P2-Pdiast)/(P1-Pdiast)$$

where Pdiast is end-diastolic pressure (Figure 1).

An AI > 100% (which often occurs on the central, but usually not on the radial pulse) indicates that reflections augment the peak systolic pressure above the level (P1) that would have been reached in their absence. A slightly different augmentation index (AIx) is calculated in the case of the central pulse only as:

$$AIx = 100 \times (P2-P1)/\text{pulse pressure}$$

where pulse pressure = max(P1, P2) – Pdiast

The AIx may be positive or negative, with a positive value indicating augmentation of peak systolic pressure by reflections.

We complemented the above calculations by computing the amplitude of diastolic reflection waves (AId), as previously described [13,14]. Briefly, the AId corresponds to the maximal distance between the upward convexity seen on the diastolic part of

the aortic or radial pressure waveform and a straight line passing through the onset of the incisura and tangent to the last diastolic part of the waveform (i.e. the vertical distance between points P3 and P4 on Figure 1). This distance is interpreted as an approximate deviation from the monoexponential decay that would be expected if there were no reflected waves in diastole. As in the case of the AIx, the AId is expressed in percent of aortic pulse pressure, i.e.

$$AId = 100 \times (P3\text{-}P4)/\text{pulse pressure}$$

Statistical analysis

Statistical analysis was carried out with repeated measures analysis of variance. The factors included in the model were the exercise session, the post-exercise time, and their interaction. To guard against an overinflation of type I errors due to potential violation of the compound symmetry assumption, omnibus F tests were made with adjusted degrees of freedom (Greenhouse-Geisser). When the omnibus test reached statistical significance, differences between the relevant pairs of means were sequentially tested using Hochberg's modification of the Bonferroni procedure, with calculations made using specific error terms (rather than the pooled mean square error), as recommended [17]. This strategy of hypothesis testing is conservative. The nominal alpha was uniformly set at 0.05. The data were summarized as mean ± SD. The calculations were made with the Stata software (release 9.0, Stata Corporation, College Station, Texas, USA).

RESULTS

Hemodynamic parameters in the course of recovery from the two exercise sessions are shown in Tables 1 and 2. As expected, heart rate progressively declined, but at the end of the 45 minutes observation period it was still higher than the baseline value recorded preexercise. From values way above baseline 5 minutes post-exercise, brachial blood pressure rapidly decreased, reaching levels at (4000 m run) or slightly below (treadmill test) the preexercise value after 25- 45 minutes of recovery. Central blood pressure followed an identical trend, with the systolic value lower than its brachial counterpart at all time points. Thus, 45 minutes after the end of either type of exercise, hemodynamic status comprised residual tachycardia, indicating incomplete cardiovascular recovery, with in addition modest hypotension in the case of the treadmill test. After this test also, residual tachycardia at 45 minutes was more marked than after the 4000 m run.

Whether derived from the radial or central pulse, the systolic AI was below baseline 5 minutes after both types of exercise, although statistical significance was not reached. The radial and central systolic AI went on declining, to reach their lowest value at 45 minutes after the end of the treadmill test (Table 1), whereas they remained essentially stable (i.e. below baseline, but without statistical significance) in the course of recovery from the 4000m run (Table 2). The AIx (calculated from the central pulse only, Figure 1 and Methods) displayed a similar behavior (Tables 1 and 2, and Figure 2, full symbols).

Whether derived from the radial or central pulse, the (diastolic) AId was also below baseline at 5 minutes post-exercise (although this difference was not statistically significant in the case of the radial AId after the 4000 m run). However, the further time course of this index was characterized by a progressive increase, to reach values clearly above the baseline level at the end of the observation period following

either session ($p<0.001$) (Tables 1 and 2, Figure 2, open symbols).

The contrasting behaviors of systolic and diastolic reflections is recognizable in the ensemble averaged pulse waveforms, shown for the case of the treadmill test in Figure 3. On the central pulse recorded in baseline, a pattern of systolic augmentation (i.e. an inflexion point *preceding* peak pressure, and thus an AI>100% and a positive AIx) is clearly visible. In the recovery period by contrast, (except at 5 minutes post exercise) the inflexion point follows peak pressure on the central waveforms, making up for an AI<100% and a negative AIx. In diastole by contrast, the upstroke above monexponential decay (accounted for by reflections) becomes progressively more prominent with the time elapsed from end of exercise, a feature visible on both the central and the radial waveform.

The AIx is known to decrease with increasing heart rate [18]. The AIx@75 is a computation carried out by the Sphygmocor software, in an attempt to correct for this confounding influence. In contrast with the AIx, the AIx@75 was higher than baseline at 5 minutes post-exercise on both sessions (Tables 1 and 2), although the difference did not reach statistical significance in the case of the 4000 m run. However, following the treadmill test, the late time courses of the corrected and uncorrected indices were similar (Table 1). 35 and 45 minutes after the end of the 4000 m run, the AIx@75 did not significantly differ from its baseline value. In a complementary approach, the AIx time course was statistically evaluated with heart rate introduced as a covariable. With this analysis, the independent effect of heart rate on the AIx amounted to a 4.3% decrease (SE 0.7%, $p<0.001$) for each 10 beats/minute increase in the case of the treadmill test. The corresponding value for the 4000 m run was 3.0 % (SE 0.7%, $p<0.001$). In either session, there were only minor quantitative and no directional differences in the time courses of the AIx@75 and the covariance-adjusted AIx.

With the same analysis of covariance just described, there was no independent influence of heart rate on either the central or the radial AId.

DISCUSSION

In the present study, we characterized in endurance-trained athletes the pattern of arterial pressure wave reflections during recovery from acute aerobic exercise. Our main new finding consists in a heretofore undescribed progressive increase in the amplitude of diastolic reflections, from below to above resting level in the course of a 45 minutes post-exercise period, noted both on the radial and on the central pulse. As a particular strength of our study, this pattern was not restricted to the laboratory setting, but was also observed in field conditions.

Two previous studies have examined the post-exercise time course of arterial pressure wave reflections in humans [10,11]. Both used radial applanation tonometry and reconstruction of the central pulse by means of a generalized transfer function as we have done. Both exclusively [10] or mainly [11] emphasized systolic events, with findings quite similar to ours in that respect. In resistance-trained and untrained healthy men, Heffernan et al. described a progressive decrease of the central AIx below the resting value in the course of a 30 minutes recovery from maximal aerobic exercise (cycle ergometer) [10]. In sedentary or recreationally active men, Munir et al. reported average values for central AIx and radial AI of respectively 1.2% and 29% 30 minutes after the end of a submaximal exercise test (peak work load 150 W on a cycle ergometer), as opposed to 6.2% and 54% preexercise ($p<0.01$ for both indices), and this decrease persisted at 60 minutes (2.9%, $p<0.05$, 31%, $p<0.05$) [11]. These data are quite consistent with our findings made in endurance-trained athletes recovering from both a maximal running test or a routine outdoor running session that was part of their training. It thus appears that a lesser contribution of reflected waves to the systolic shape of radial and central aortic pressure pulses is a general feature of hemodynamic recovery following acute aerobic exercise in healthy men, independent of exercise type, intensity, or training status.

The central AIx is known to be negatively correlated with heart rate [18], which had not yet returned to baseline at the end of the 45 minutes observation period (Tables 1 and 2). Thus, the lower AIx observed during recovery, in comparison with the preexercise value, could be related, at least in part, to residual tachycardia. Tachycardia is believed to lower the central AIx by reducing ejection duration, and thus altering the relative timing of the forward systolic and reflected pressure waves, such that the latter does not reach the central aorta in time to augment the forward systolic peak. If this factor alone was sufficient to fully account for the post-exercise time course of the AIx, the index should have progressively increased as heart rate became closer to the resting value, but we observed the opposite (Figure 3), and so did Heffernan et al and Munir et al. [10,11]. In addition, the recovery time-course of central systolic augmentation was not altered when the AIx was expressed as the value expected at a fixed heart rate (i.e. the AIx@75 as calculated by the Sphygmocor software) or when the data were analyzed with heart rate introduced as a covariate. Finally, the forward and reflected systolic waves are better separated in the radial artery than they are in the aorta (P1 and P2 in Figure 1), so that the radial systolic AI does not depend on a variable degree of overlap between these two waves. The radial systolic AI followed a time-course similar to that of the central AIx during the recovery from both exercise sessions. Heffernan et al. did not report the radial AI [10], but Munir et al. did and found results consistent with ours [11]. These aggregated observations of pulse wave morphology in the course of recovery from acute aerobic exercise point to a progressive reduction in the amplitude of the reflected pressure waves present in at least some large arteries during the systolic part of the cardiac cycle.

The post-exercise reduction in various indices of wave reflection, all calculated in systole, may be due to a generalized attenuation of reflections throughout the arterial

tree. Alternatively, the spatial distribution of reflection sites and conduction velocities may be altered in such a way that the largest part of reflected pressure energy reaches the central vessels after closure of the aortic valve. The former possibility is likely to be prevalent within the first few minutes of recovery, as shown by the concurrent fall of both systolic (AIx) and diastolic augmentation (AId) between baseline and 5 minutes post-exercise (Figure 3). With pulsatile pressure and flow in a branched system of elastic tubes, reflections are generated at sites of discontinuities (mismatch) in characteristic impedance, a function of local tube compliance and geometry (Nichols and O'Rourke, 2005). In man and in resting conditions, such sites are probably spread out throughout the arterial tree [6], with particular roles for the resistant part of the microvascular networks, and for transitions from compliant elastic vessels to less compliant muscular ones [9]. Generalized vasodilation obtained in both muscular conduit arteries and resistance arterioles by administration of organic nitrates has been found to blunt reflected pressure waves [11,19], the likely cause being a general leveling out of impedance mismatch (Nichols and O'Rourke, 2005), and a similar mechanism could be active early on in post-exercise recovery.

However, a different explanation is required for the later reappearance and overshooting of diastolic reflections, while those occurring in systole keep waning (Figure 3), at a time when hemodynamic recovery is still incomplete as shown be the residual tachycardia at 45 minutes (Tables 1 and 2). The time frame within which the AId progressively increased in the present study is consistent with the time-course of systemic vascular resistance reported in healthy humans recovering from aerobic exercise by Kilgour et al [20], but we need a further ingredient to account for the overshooting. This might be provided by studies of post-exercise pulse wave velocity in conduit arteries (PWV). In 12 male sedentary male volunteers recovering from 30 minutes of bicycling at 60% VO2max, Kingwell et al. observed a 10% decrease, with

respect to preexercise value, in leg PWV assessed from simultaneous recording of pulse over the femoral and dorsalis pedis arteries [4]. The corresponding decrease of aortic PWV (carotid to femoral) was much less (4%). In the same kind of subjects, leg and arm PWV were remaining at 10% below their baseline value 60 minutes after termination of a maximal running test (i.e. carried out to VO2max, on a treadmill, as in the present work) [5]. Finally, in the aforementioned study by Munir et al, aortic PWV (carotid to femoral) was unchanged from preexercise throughout 60 minutes of recovery from a submaximal treadmill test [11]. Because PWV is inversely related to vessel compliance [6], these aggregated data are simply explained by the greater impact of persisting low smooth muscle tone on the mechanical properties of peripheral muscular, as opposed to central elastic arteries. One result may be a persistent blunting of reflection-generating impedance mismatch at the transition between these two types of vessels. To account for the recovery time course of reflected waves observed on the central pulse in the present study (Figure 3), the following scheme could therefore be proposed. As resistance vessels in skeletal muscle progressively (although yet incompletely) recover their resting tone, generation of reflected pressure waves resumes at these sites, but theire backwards conduction remains slowed along peripheral muscular conduit arteries. At the same time, reflections at more proximal sites (i.e. more likely to top up systolic central pressure because of a shorter transmission path) remain weak, due to persistent better impedance matching at the elastic-muscular transition of conduit arteries. As a result, the reflected waves reaching the aorta concentrate in diastole. The overshoot of the diastolic wave above the preexercise value observed after 45 minutes of recovery is reminiscent of the high amplitude diastolic waves described on the central pulse of the kangaroo, which was attributed to a particularly low spatial dispersion of arterial reflection sites in this species [21].

Our results, as well as those of the studies cited above, imply that conductance arteries undergo transient changes in stiffness in the course of post-exercise recovery. Such changes could be mediated by smooth muscle relaxation induced by endothelial release of vasodilators as a consequence of increased blood flow and shear stress [4]. Relaxation of smooth muscle may decrease the stiffness of the vascular wall either directly (i.e. a reduced elastic modulus of the smooth muscle material itself) or indirectly (i.e. a transfer of the load normally borne by stiff collagen fibers, mounted in series with smooth muscle cells, to the more compliant elastin fibers, which are arranged in parallel with muscle elements [6,16].

Limitations

We have only recorded the arterial pulse, and therefore had to base our interpretation in part on post-exercise arterial mechanics data collected by others in similar circumstances. Thus, the scheme just outlined, although coherent with our observations on the diastolic part of the pulse waveform, needs confirmation. Furthermore, it probably represents an oversimplification, because it does not account for the progressive decline in AIx observed following the treadmill test, nor why this decline is less marked after the 4000 m run (Figure 2). We acknowledge that we have no explanation for this part of our data. However, it makes intuitive sense that a variable which during recovery deviates from its baseline value should do so more markedly following a more intense exercise.

In addition, some have challenged the validity of the generalized transfer function (GTF) approach for reconstructing the central arterial from the radial pulse in or shortly following exercise, due to the fact that the associated changes in vascular tone in the upper limb may of themselves modify the GTF with respect to its resting pattern [22,23,24]. However, in the only available direct comparison carried out in

humans during – admittedly submaximal – exercise, the shapes of the invasively measured and reconstructed aortic pulse were superimposable [25]. In further support for the validity of the noninvasive reconstruction carried out here, the dependence of the AIx on heart rate was qualitatively identical, and quantitatively very close to that found by Wilkinson et al. [18] following an analysis of reconstructed central waveforms obtained in resting patients whose pulse rate was manipulated with cardiac pacing (decrease in AIx per 10 b/min increase in heart rate found by these authors: 3.9 %; present study, after adjustment for time post-exercise: 4.3% for treadmill.max or 3 % for 4000 m submax).

As a last remark, Munir et al in their aforementioned study [11] found a time course of the radial diastolic augmentation index (the aortic one was not calculated) not in accordance with that shown in Tables 1 and 2, in that values remained below the preexercise level at all times of recovery. Thus, these authors apparently did not observe, as we did, an overshoot in the amplitude of the diastolic reflection wave. Referring to Figure 1 however, their calculation of diastolic augmentation was $100\times$(P3 – Pdiast)/PP rather than the formula shown for our AId, thereby encompassing two components of diastolic pressure, one related to the monoexponential decay expected in absence of reflections, and the other one due to the reflected wave. In contrast, we attempted to capture only the latter. From our data, we recomputed the radial diastolic AI with Munir's formula and also failed to observe an overshoot (Table 3).

Finally, the present observations have been exclusively made in young subjects. With advancing age, the shape of the central aortic pressure waveform in the resting state undergoes marked changes: due in part to increased stiffness and pulse wave velocity of elastic conduit arteries, pressure augmentation by reflections progressively gains importance in systole and loses it in diastole [7]. Whether and

how this pattern would be acutely affected by exercise in elderly subjects remains to be determined.

Perspectives

We have provided a description in healthy humans of evolving central pulse modifications by reflected pressure waves during recovery from acute aerobic exercise. This description encompasses for the first time not only systolic, but also diastolic events. Beyond the first few minutes following exercise termination, where pressure augmentation by reflected waves appears markedly blunted or entirely absent, reflections selectively reappear on the diastolic part of the central pulse, with an amplitude at times exceeding that in the resting state. This phenomenon, whose determinants remain to be evaluated rigorously, might contribute to the maintainance of coronary perfusion pressure in the face of post-exercise hypotension.

ACKNOWLEDGMENTS

The authors wish to thank all staff at the Service de Médecine du sport, who helped with exercise testing.

The present study was exclusively funded by departmental funds, and not by any external source.

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TABLE 1

	minutes post-exercise					
	BL	5	15	25	35	45
Heart rate (b/min)	64 ± 8	98 ± 11 **	93 ± 9 **†	89 ± 10 **†	84 ± 9 **	82 ± 12 **†
Ejection duration (msec)	295 ± 18	261 ± 21 **	269 ± 16 **†	269 ± 13 **	274 ± 14 **	274 ± 17 **
Brachial blood pressure (mm Hg)						
Systolic	127 ± 9	171 ± 19 **	127 ± 12	117 ± 9	116 ± 7 **	114 ± 7 **
Diastolic	78 ± 8	85 ± 11	74 ± 4	73 ± 5	72 ± 5	72 ± 6 *
Mean	93 ± 7	112 ± 12 **	91 ± 5	87 ± 6	85 ± 5 **	85 ± 6 **
Pulse	49 ± 9	85 ± 17 **	53 ± 12	44 ± 7	44 ± 6	42 ± 5 *
Central blood pressure (mm Hg)						
Systolic	110 ± 9	138 ± 14 **	106 ± 7	100 ± 7 *	99 ± 5 **	97 ± 6 **
Diastolic	79 ± 8	89 ± 11	77 ± 5	75 ± 5	74 ± 5 *	73 ± 6 **
Mean	93 ± 7	112 ± 12 **	91 ± 5	87 ± 6	85 ± 5 **	85 ± 6 **
Pulse	31 ± 7	49 ± 11 **	29 ± 7	25 ± 5	25 ± 4 *	24 ± 3 *
P1	107 ± 7	136 ± 14	106 ± 7	100 ± 7	98 ± 5 **	97 ± 6 **
Reflection indices from radial pulse						
Systole						
AI (%)	56 ± 12	52 ± 9	45 ± 7 *	43 ± 5 *	42 ± 8 *	42 ± 8 **
Diastole						
AId (%)	16.8 ± 4.7	12.8 ± 4.5 *	18.7 ± 5.4	23.1 ± 4.8 **	24.9 ± 6.3 **	25.9 ± 7.6 **
Reflection indices from central pulse						
Systole						
AI (%)	107 ± 11	101 ± 8	96 ± 6 **†	95 ± 5 **	94 ± 6 **	93 ± 6 **
AIx (%)	5.8 ± 9.5	0.5 ± 7.3	-4.2 ± 5.9 **†	-5.5 ± 4.5 **	-5.7 ± 6.0 **	-7.3 ± 6.4 **
AIx@75 (%)	0.6 ± 8.5	10.3 ± 4.1 **	4.4 ± 4.1	1.1 ± 5.8	-1.2 ± 7.1	-4.2 ± 5.0 *
TT (msec)	48 ± 10	35 ± 7 **	33 ± 4 **	30 ± 7 **	33 ± 6 **	36 ± 5 **
Diastole						
AId (%)	6.8 ± 3.2	2.0 ± 2.2 **	5.4 ± 2.9	8.0 ± 2.1	9.6 ± 4.1 **	10.1 ± 4.1 **

Hemodynamic and wave reflection parameters in the course of recovery from maximal aerobic exercise (treadmill test)
BL baseline values recorded pre-exercise. Definitions of other abbreviations: see Methods and Figure 1. Data are means ± SD, n = 11.
*p<0.05, **p<0.01 vs BL. † p<0.05 vs submaximal aerobic exercise (4000 m run).

TABLE 2

	minutes post-exercise					
	BL	5	15	25	35	45
Heart rate (b/min)	62 ± 10	95 ± 8 **	84 ± 10 **	80 ± 10 **	76 ± 10 **	74 ± 11 **
Ejection duration (msec)	299 ± 18	273 ± 21 **	285 ± 16 *	286 ± 13 *	286 ± 14 *	288 ± 17 **
Brachial blood pressure (mm Hg)						
Systolic	119 ± 12	171 ± 20 **	123 ± 9	115 ± 12	114 ± 11	117 ± 9
Diastolic	76 ± 5	87 ± 10 *	73 ± 8	72 ± 7	71 ± 8	71 ± 9
Mean	90 ± 7	116 ± 11 **	90 ± 8	86 ± 8	84 ± 9	85 ± 10
Pulse	43 ± 10	84 ± 19 **	50 ± 9	43 ± 8	43 ± 7	46 ± 8
Central blood pressure (mm Hg)						
Systolic	105 ± 12	139 ± 15 **	106 ± 10	99 ± 11	98 ± 10	100 ± 10
Diastolic	77 ± 5	91 ± 10 **	75 ± 7	74 ± 7	72 ± 8	72 ± 9
Mean	90 ± 7	116 ± 11 **	90 ± 8	86 ± 8	84 ± 9	85 ± 10
Pulse	29 ± 10	48 ± 12 **	31 ± 7	26 ± 6	26 ± 5	28 ± 7
P1	102 ± 8	137 ± 13 **	103 ± 8	98 ± 9	97 ± 9	98 ± 8
Reflection indices from radial pulse						
Systole						
AI (%)	57 ± 18	51 ± 8	54 ± 11	53 ± 11	51 ± 14 *	50 ± 17
Diastole						
AId (%)	15.6 ± 7.6	14.2 ± 8.0	18.9 ± 9.8 *	21.2 ± 10.0 **	22.5 ± 10.9 **	22.1 ± 9.2 **
Reflection indices from central pulse						
Systole						
AI (%)	111 ± 17	102 ± 8	107 ± 11	102 ± 11	101 ± 11	103 ± 15
AIx (%)	8.2 ± 14.7	1.6 ± 7.3	5.9 ± 9.7	1.1 ± 10.0	0.2 ± 10.5	2.1 ± 13.2
AIx@75 (%)	2 ± 12	11 ± 7	10 ± 8	3 ± 7	1 ± 7	1 ± 11
TT (msec)	54 ± 10	39 ± 10 **	42 ± 11 **	40 ± 10 **	41 ± 9 **	44 ± 14 *
Diastole						
Aid (%)	7.3 ± 4.4	3.5 ± 4.3 *	6.4 ± 5.7	8.1 ± 5.6	9.2 ± 6.7	9.5 ± 5.4 *

Hemodynamic and wave reflection parameters in the course of recovery from sub maximal aerobic exercise (4000 m run)
BL baseline values recorded pre-exercise. Definitions of other abbreviations: see Methods and Figure 1. Data are means ± SD, n = 11.
*p<0.05, **p<0.01 vs BL.

TABLE 3

		minutes post-exercise			
Munir et al.	BL	1-3	15	30	60
	37 ± 9	11 ± 7**	25 ± 15**	29 ± 10**	31 ± 14**
This study	BL	5	15	25	45
treadmill-max	45 ± 3	25 ± 5**	31 ± 5**	34 ± 4**	39 ± 3**
4000m-submax	44 ± 6	28 ± 6**	37 ± 5*	39 ± 3	42 ± 5

Radial diastolic augmentation index calculated as described by Munir et al (Munir et al., 2008), and expressed in percent of pulse pressure. BL baseline values recorded pre-exercise. *Treadmill-max*: indoor treadmill run to maximal aerobic capacity *4000m-submax* outdoor 4000 meters run. * $p<0.05$, ** $p<0.01$ vs BL. Errors are SD, recalculated in the case of the first table line from the SE and n provided in (Munir et al., 2008).

LEGENDS TO FIGURES

Figure 1

Points used to characterize systolic and diastolic reflected waves on the central and radial pressure pulse.

The long broken line designates end-systole. Pdiast diastolic pressure. P1 peak of forward systolic wave. P2 peak of systolic reflected wave P3 peak of diastolic reflected wave. ΔT time lag between peaks of systolic reflected and forward waves, TT transmission time of systolic reflected wave. A straight line tangent to the diastolic part of the waveform is drawn as shown in order to delineate the diastolic reflected wave. P4 approximates the pressure that would exist at the time of P3 in absence of reflection. Indices of wave reflection are calculated from the pressures at points P1 to P4 according to the formulas shown, where PP is pulse pressure. See Methods.

Figure 2

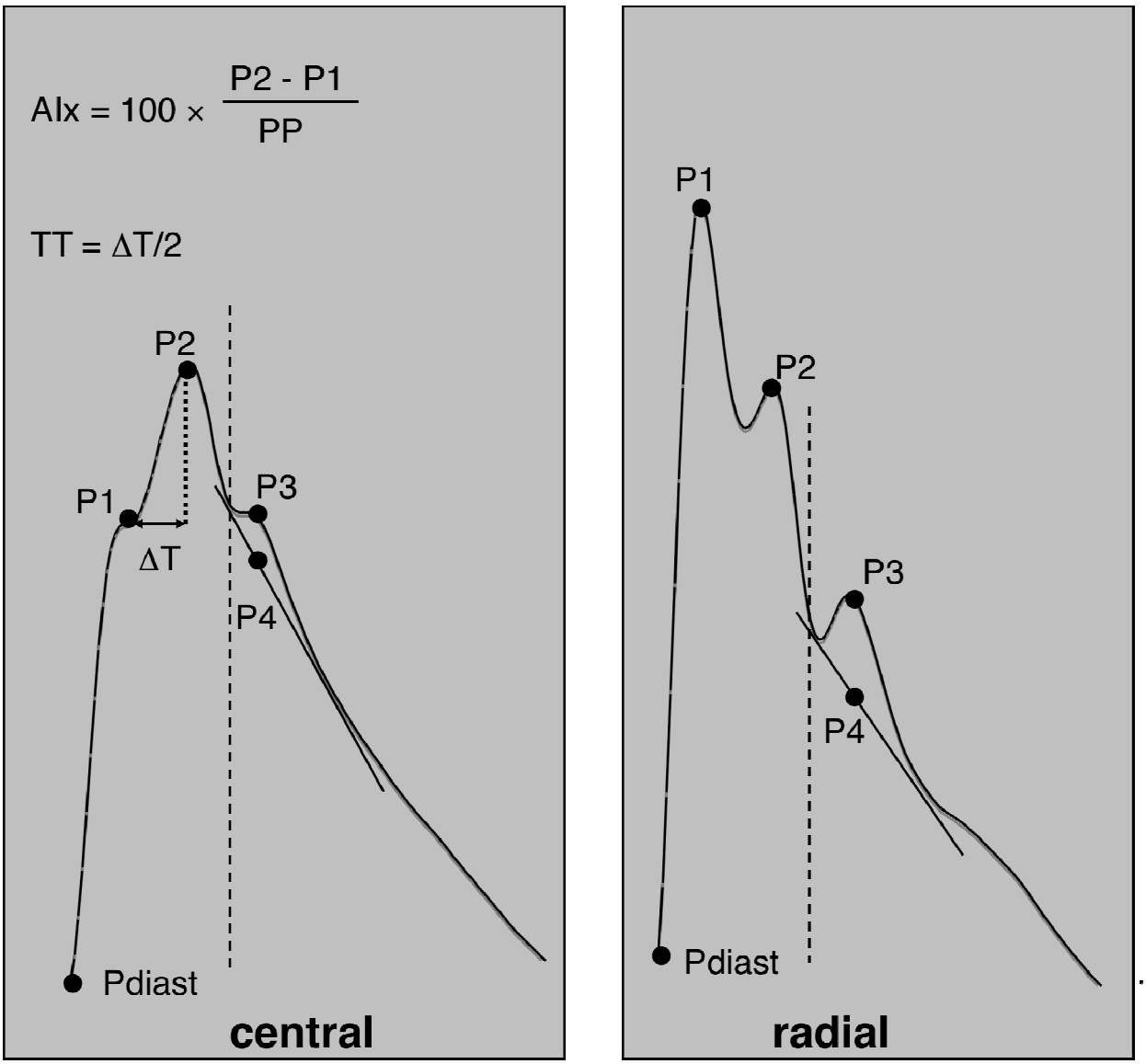
Central systolic and diastolic augmentation indices in the course of recovery from either maximal or submaximal aerobic exercise

Definitions of AIx and AId: see Figure 1 and Methods. *Treadmill-max*: indoor treadmill run to maximal aerobic capacity *4000m-submax* outdoor 4000 meters run. BL baseline values recorded pre-exercise * $p<0.05$, ** $p<0.01$ vs BL. † $p<0.05$ vs submaximal aerobic exercise. Mean and SE, 11 subjects.

Figure 3

Ensemble-averaged central and radial pressure waveforms in the course of recovery from maximal aerobic exercise

BL baseline waveform recorded preexercise. Numbers in italics designate minutes elapsed from end of exercise.



$$AI = 100 \times \frac{P2 - Pdiast}{P1 - Pdiast}$$

$$AId = 100 \times \frac{P3 - P4}{PP}$$

FIGURE 1

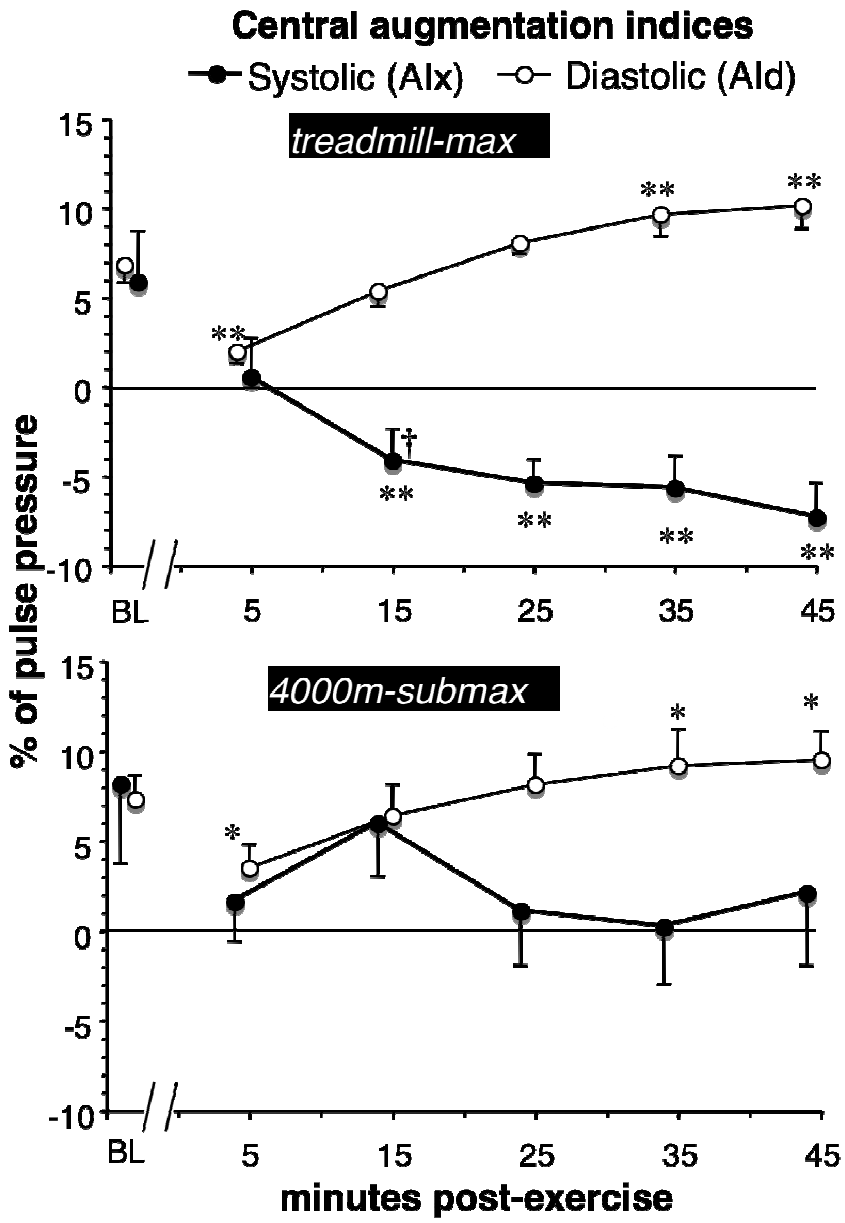

Central augmentation indices
Systolic (AIx)
Diastolic (AId)
treadmill-max
4000m-submax
% of pulse pressure
minutes post-exercise
BL
5
15
25
35
45
15
10
5
0
-5
-10

FIGURE 2

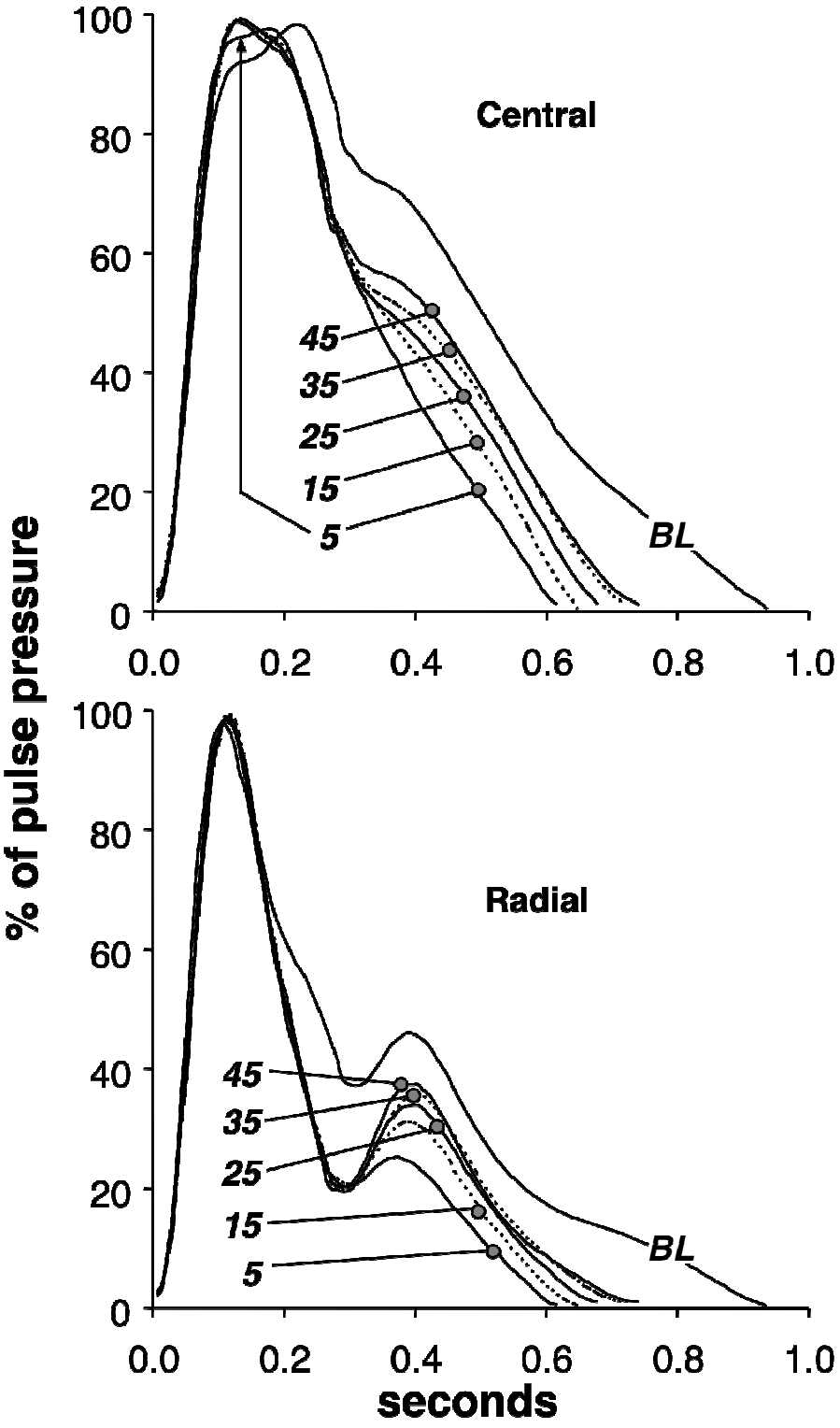

Central
Radial
45
35
25
15
5
BL
% of pulse pressure
seconds
0
20
40
60
80
100
0.0
0.2
0.4
0.6
0.8
1.0

FIGURE 3