ORIGINAL REPORT

Diastolic retrograde arterial flow: Preliminary report☆

M.J. Mc Loughlin *, S. Mc Loughlin, J. Milei

Instituto de Investigaciones Cardiológicas Alberto C. Taquini (ININCA) UBA-CONICET, Buenos Aires, Argentina

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KEYWORDS
Retrograde flow; Reflux; Doppler

Abstract

Objective: Holodiastolic arterial blood flow is associated with pathological conditions. Nevertheless, we have observed that lifting the arm at an angle greater than the horizontal causes holodiastolic arterial blood flow in the brachial artery in normal patients. Thus, we decided to assess the frequency and characteristics of this phenomenon.

Material and methods: Ten volunteers (7 women) aged 43 ± 17 years participated in the study. We used an ultrasound scanner with a 12 MHz probe to analyze the brachial artery. The examination included: (a) baseline measurements in the supine position; (b) measurements during 3 min with the arm raised; and (c) a measurement 60 s after lowering the arm to the supine position in which the baseline measurements had been obtained.

Results: We observed mid- and end-diastolic retrograde flow in 8/10 patients when their arms were raised. No mid- or end-diastolic retrograde flow was observed in the baseline measurements or after the arm was lowered to the supine position (p = 0.0007). The minimum diastolic velocity was significantly higher in the measurements obtained with the arm raised than in the supine position before or after arm raising (−13.5 ± 4.9 cm/s vs −2.38 ± 7.5 cm/s, p < 0.05 and −13.5 ± 4.9 cm/s vs −4.6 ± 5.2 cm/s, p < 0.05, respectively). The modified resistance index was significantly higher when the arm was raised (1.20 ± 0.07 vs 1.04 ± 0.15; p < 0.05); moreover, the modified resistance index was significantly lower in the measurements obtained after the arm was lowered than in the baseline measurements (1.20 ± 0.07 vs 1.07 ± 0.08; p < 0.05).

Conclusion: We conclude that holodiastolic reflux occurs in healthy patients. This physiological phenomenon merits further investigation and can help elucidate previous observations in different pathological conditions.

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Flujo retrógrado diastólico. Comunicación preliminar

**Resumen**

**Objetivo:** La existencia de flujo sanguíneo arterial retrógrado holodiastólico es un fenómeno asociado a condiciones patológicas. Sin embargo, hemos observado que en pacientes sanos, la elevación del brazo por encima de la horizontal produce flujo de estas características en la arteria braquial. Por lo tanto, decidimos evaluar la frecuencia y características de dicho fenómeno.

**Material y métodos:** Diez voluntarios (7 mujeres) con una edad de 43 ± 17 años participaron del estudio. El análisis de la arteria braquial fue realizado utilizando un equipo de ultrasonido con transductor de 12 MHz. El estudio incluyó: a) mediciones basales en posición supina; b) una evaluación de 3 minutos con el brazo elevado, y c) una medición a los sesenta segundos después de bajar el brazo a la posición supina en la cual fueron realizadas las mediciones basales.

**Resultados:** Se encontró flujo retrógrado meso y telediastólico en 8/10 pacientes durante la elevación del brazo. En las mediciones basales y post-elevación ningún paciente presentó flujo retrógrado (p = 0,0007). La velocidad mínima diastólica se incrementó significativamente durante las mediciones con el brazo elevado en comparación con aquellas basales y post-elevación (−13,5 ± 4,9 cm/s frente a −2,38 ± 7,5 cm/s; p < 0,05 y −13,5 ± 4,9 cm/s frente a −4,6 ± 5,2 cm/s; respectivamente; p < 0,05). El índice de resistencia modificado presentó un aumento significativo durante la elevación del brazo (1,20 ± 0,07 frente a 1,04 ± 0,15; p < 0,05) y un descenso significativo en las mediciones post-elevación comparado con aquellas basales (1,20 ± 0,07 frente a 1,07 ± 0,08; p < 0,05).

**Conclusión:** Concluimos que el flujo holodiastólico está presente en pacientes sanos. La comunicación de este nuevo fenómeno fisiológico fomenta futuras investigaciones y podría ayudar a comprender observaciones previas en distintos estados patológicos.

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**Introduction**

Despite the major advances made over the last century, cardiovascular disease remains the leading cause of death in Western societies. Endothelial dysfunction and arterial stiffness are considered early factors in the development of cardiovascular diseases. Ultrasound assessment of the flow-mediated dilatation and analysis of arterial blood pressure have been established as valid and reliable tools to identify patients who need early intervention. Infectious, chromosomal and physical mechanisms that affect vascular integrity have also been studied. As far as the physical mechanisms are concerned, shear rate (8. mean rate/diameter) is associated with endothelial dysfunction. Curiously enough, atherosclerotic lesions are mostly located in areas with oscillatory flow (bidirectional blood flow) and mid-low shear stress. In addition, retrograde shear rate induces a dose-dependent attenuation of endothelial function in humans. Endothelial-dependent vasodilation of the brachial artery is attenuated by increased hydrostatic pressure and reduced shear rate. Diastolic retrograde flow in the brachial artery in young patients during meso- and end-diastole is often associated with diseases such as subclavian steal syndrome. When we observed by chance the presence of meso- and end-diastolic retrograde flow in the brachial artery of healthy young individuals when they lifted their arms, and taking into consideration the potentially harmful repercussion of this hemodynamic pattern, we decided to further examine the frequency of diastolic retrograde flow in the brachial artery and its characteristics. For this purpose, blood flow velocity, resistance index, and pulsatility index were measured. It was also determined whether meso- and end-diastolic retrograde flow occurred at baseline with the patients’ arms raised, and then lowered. The study was approved by the University of Buenos Aires and it complied with the Declaration of Helsinki. The subjects were informed of the procedures and risks of the study and all gave informed consent. Ten individuals (seven women) volunteered to participate in the study. They were all healthy, and had no previous history of hypertension, diabetes or vascular disease. None of them was under medication, including oral contraceptives. They were instructed to fast and refrain from exercise for 12 h and alcohol for 48 h. They rested in the supine position for 20 min before imaging, as indicated in a previous paper.

**Methods**

The hemodynamic study was performed in one single session. Normal arterial pressure was confirmed by indirect determination in the left arm prior to Doppler US evaluation. The examination to visualize the humeral artery approximately 5 cm proximal to the antecubital fossa in the longitudinal plane was performed using a standard ultrasound scanner with a 12 MHz probe. Doppler flow velocity data were acquired with an insonation angle <50°. The wall filter was set at the lowest possible level (50 Hz). A 1 mm sample volume and a duplex scanning technique combining B-mode and Doppler imaging were used to ensure that venous signals were not registered. Calculations, made with a built-in software programme, included the following parameters: peak systolic velocity, minimum diastolic velocity, pulsatility index, and modified resistance index (peak systolic velocity minus minimum diastolic velocity divided by peak systolic velocity). Mean flow velocity was quantified...
Table 1  Doppler US measurements.

<table>
<thead>
<tr>
<th></th>
<th>PSV (cm s⁻¹)</th>
<th>MDV (cm s⁻¹)</th>
<th>MRI</th>
<th>PI</th>
<th>Mean vel. (cm s⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>72.34 ± 34</td>
<td>−2.38 ± 7.5</td>
<td>1.04 ± 0.15</td>
<td>6.77 ± 4.9</td>
<td>13.2 ± 6.7</td>
</tr>
<tr>
<td>With the arm raised</td>
<td>69.6 ± 28</td>
<td>−13.5 ± 4.9</td>
<td>1.20 ± 0.07</td>
<td>10.6 ± 4.1</td>
<td>9.3 ± 5.2</td>
</tr>
<tr>
<td>With the arm lowered</td>
<td>74.0 ± 29</td>
<td>−4.6 ± 5.2</td>
<td>1.07 ± 0.08</td>
<td>5.6 ± 1.8</td>
<td>15.4 ± 8.11</td>
</tr>
</tbody>
</table>

n = 10. The values correspond to mean ± SD.
SD, standard deviation; PI, pulsatility index; MRI, modified resistance index; n, sample size; MDV, minimum diastolic velocity; Mean vel., mean velocity; PSV, peak systolic velocity.

by calculating peak systolic velocity minus minimum diastolic velocity divided by pulsatility index. The right arm was used in all cases. The patient, in the supine position, the right arm was raised, and then, lowered for baseline measurement. The hemodynamic study involved the following: (a) baseline measurement; (b) 3-min measurement with the right arm raised; and (c) 60-s measurement immediately after lowering the arm until reaching baseline. Baseline images and images after arm elevation were acquired with the patient in the supine position and the arm on the examination table. After baseline measurement, the patient’s arm was passively raised to 90°, an angle perpendicular to the examination table. This angle was used to minimize any possible muscular effort. Meso- and end-diastolic retrograde flow did not always remain constant during the 3-min in which the patient’s arm was raised. Meso- and end-diastolic retrograde arterial flow was considered negative when it remained undetected during the 3-min measurement. In patients with a positive meso- and end-diastolic retrograde flow, measurements were based on the best signal acquired during the period in which the patient kept the arm up. SPSS software (version 18.0) was used for statistical analysis. Continuous variables were presented as mean ± standard deviation and ANOVA with post hoc comparison was also used. Categorical variables were compared using the bilateral Fisher’s exact test.

Results

The participants’ mean age was 43 ± 17 (mean ± SD). Mean weight was 65 ± 11 kg and BMI was 24.5 ± 3. Pulse pressure prior to the hemodynamic study was 37.9 ± 9.95 mmHg. Mean heart rate was 72 ± 81 bpm, 73 ± 61 bpm, and 73 ± 81 bpm in baseline measurements, measurements with the arm raised, and measurements with the arm lowered, respectively. Minimum diastolic velocity increased significantly with the arm raised in contrast with baseline measurements and measurements with the arm lowered (−13.5 ± 4.9 cm/s against 2.38 ± 7.5 cm/s; p < 0.05 and −13.5 ± 4.9 cm/s against 4.6 ± 5.2 cm/s; p < 0.05). The modified resistance index increased significantly while the arm was raised, in contrast with baseline measurements (1.20 ± 0.07 against 1.04 ± 0.15; p < 0.05), and it decreased significantly after arm lowering (1.20 ± 0.07 against 1.07 ± 0.08; p < 0.05). Table 1 includes the mean Doppler measurements. Regarding the non-parametric characteristics, the meso- and end-diastolic retrograde arterial flow was positive in 0/10 patients at baseline measurements. During the 3 min with their arms raised, 8/10 patients (p = 0.0007) showed a positive meso- and end-diastolic retrograde flow. Back to baseline position of the arm, 0/10 patients showed no diastolic retrograde arterial flow (Fig. 1).

Discussion

Previous studies reported an increased diastolic retrograde flow in the arterial artery of elderly patients having one or two cardiovascular risk factors. Similar studies of other vascular beds (e.g., the external iliac artery) have reported a meso- and end-diastolic retrograde flow in healthy elderly subjects in the supine position. Explanations for these findings are an increase in vascular impedance caused by a hyper-adrenergic state, hormonal influences, or a decrease in the production of nitric oxide (NO). Our findings demonstrated the presence of a meso- and end-diastolic retrograde flow in the brachial arteries of a healthy and young population. Thijssen has also shown that a diastolic retrograde arterial flow can be induced by using arm cuff inflation at different pressures.
Although the G-force might not be the only factor having a bearing on our findings, the presence of diastolic retrograde arterial flow when the arm is raised suggests that the G-force plays a major role. We think that the observation of diastolic retrograde arterial flow throughout diastole is a manifestation of the interaction between the diastolic driving forces and the hydrostatic force exerted by the total blood column. The degree and distribution of the diastolic retrograde flow of the brachial artery in the entire arterial tree were not taken into consideration. However, we suggest that the driving and gravitational forces could be similar at a particular point in the arterial tree, thus preventing a higher diastolic retrograde arterial flow. This point could be proof of the efficiency of arterial diastolic function, arterial recoil (Windkessel effect), and arterial stiffness.

It should be noted that although the protodiastolic reflux in the muscular arteries is a common finding (triphasic flow), the meso- and end-diastolic retrograde flow establishes a qualitative difference between baseline measurements and measurements with the arm raised. Unlike in the analysis of blood flow velocity, this characteristic may be independent from the insonation angle, which is a relevant aspect because Doppler US measurements with insonation angles >30° show a significantly high variability.

A major limitation of our study is that the sample volume was set at 1 mm. Since the flow velocity profile in the brachial artery is usually parabolic, the instantaneous peak and minimum velocities acquired could fail to be indicators of the total flow velocity, only showing the characteristics of the laminar flow of the central circulation. However, the lowest possible sample volume was chosen in order to minimize the venous signals that might exaggerate or simulate a retrograde arterial flow during arm elevation. The disappearance of diastolic retrograde arterial flow during the 3-min measurement with the arm raised can be explained by the difficulty in detecting low flow velocities. In addition, variability of the diastolic retrograde arterial flow was observed during inhalation and exhalation throughout the 3-min measurement.

In conclusion, the correlation between our findings and those reporting an association of the diastolic retrograde arterial flow with advanced age and cardiovascular risk factors shows that this condition can be detected in the healthy population. Detection of diastolic retrograde arterial flow with sensitivity methods (e.g., progressive gravitational force and cuff inflation) is promoting a new technique, which draws on flow-mediated dilation or intima-media thickness, for early evaluation of vascular function. Unlike evaluation of flow-mediated dilation or intima-media thickness, detection of diastolic retrograde arterial flow does not require the use of a supplemental software program.

Future research will be able to look into the effects of inverse shear rate on endothelial function and into the influence of arterial stiffness and breathing movements on diastolic retrograde arterial flow.

**Conflict of interest**

The authors declare not having any conflict of interests.

**Authorship**

1. Responsible for the integrity of the study: MJMCL.
2. Conception of the study: MJMCL, SMCL.
3. Design of the study: MJMCL, SMCL.
4. Acquisition of data: MJMCL.
5. Analysis and interpretation of data: MJMCL, SMCL, JM.
6. Statistical analysis: MJMCL, SMCL.
7. Bibliographic search: MJMCL, SMCL.
8. Drafting of the manuscript: MJMCL, SMCL.
9. Critical review with intellectually relevant contributions: JM.
10. Approval of the final version: MJMCL, SMCL, JM.

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**References**


