**Invasive validation of the Complior Analyse in the assessment of central artery pressure curves: a methodological study**

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**Introduction**

Arteries are the target, the place, and the common denominator of cardiovascular diseases; hence, study of arterial function is of greatest importance in clinical practice. The aim of this study was to evaluate the accuracy of carotid pulse wave analysis using the new version of the Complior device – the Complior Analyse.

**Methods and results**

This was a cross-sectional study that included 15 patients (seven women), mean age 62.07 ± 10.59 years, referenced for cardiac catheterization. Pressure curves were obtained simultaneously in the ascending aorta (invasively) and in the right common carotid artery (using the Complior Analyse). Mean central arterial pressures, augmentation indexes, and wave morphology obtained using both methods were compared. A good concordance between methods was obtained for all the parameters measured, with intraclass correlation coefficients above 0.9. Bland–Altman analysis also indicated a good accuracy profile of the Complior device, with small mean differences observed for all parameters and most values confined within 2 SD of the mean difference. This was further confirmed by the strong Pearson correlation coefficients, with \( r \) coefficients above 0.92 for all the variables studied. The correlations observed were independent of sex, age, arterial pressure, and BMI.

**Conclusion**

The results presented and available research clearly indicate that the Complior Analyse device measures carotid pressure waves accurately; therefore, it is a simple and reliable noninvasive alternative for pressure wave analysis. *Blood Press Monit* 00:000–000 © 2014 Wolters Kluwer Health | Lippincott Williams & Wilkins.

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**Introduction**

Cardiovascular diseases are the main cause of death and morbidity worldwide, making its prevention, diagnosis and treatment a major topic of research and discussion within the medical and scientific community [1].

The study of arterial physiopathology has reached a level of great importance, given the fact that arteries are the place, the target, and the common denominator of cardiovascular diseases [2–6].

Measurement of peripheral arterial pressure over the brachial artery remains the most common and widely used method for the evaluation of arterial hemodynamics in clinical practice, assuming a distinguished role in the prediction of cardiovascular morbidity and mortality [7]. Still, and because of the proximity to the heart and the significant differences between the peripheral and central arterial systems, central arterial pressure may be a better indicator for the quantification of cardiovascular risk and for therapeutic optimization [7–17]. In fact, several studies have reported significant discrepancies among different antihypertensive drugs, translating into higher rates of cardiovascular events whenever the benefit in terms of central arterial pressure was reduced, even when a similar reduction in peripheral arterial pressure was obtained [8–11,14]. These results indicate that the ventricular–vascular interaction cannot be inferred by the peripheral arterial pressure, taking into account the pressure amplification that occurs from the heart to the periphery, as a consequence of the variations in vascular impedance all along the arterial system [4,7,12,13,15–17]. However, there is clear evidence on the degenerative effects of aging on the central arteries, producing marked changes in all the ventricular–vascular interaction parameters, with little or no influence on the peripheral arterial pressure curve [9,17,18].

Considering the accumulated evidences, the study of central arterial function constitutes a fundamental aspect of global cardiovascular risk quantification, mainly through measures of arterial stiffness (particularly aortic pulse wave velocity) and central pulse wave analysis. A methodological challenge that has been pursued is the development of noninvasive options for the measurement and study of central arterial pressure curves [19–31]. In this respect, several devices have been developed that derive the central pressure curve from the pressure wave at the carotid and/or radial arteries. Among these methods, applanation tonometry has been recognized as the standard noninvasive method. This
methodology has been found to be reproducible, although its dependence on mathematical transfer functions may well translate into important calibration errors, limiting its potential clinical use [32–37].

More recently, a new device has been made available (Complior Analyse), allowing for the traditional aortic pulse wave velocity measurement through simultaneous carotid–femoral pulse recording as in previous Complior device versions, but concurrently recording the carotid arterial pressure curve and estimating central pressure wave parameters directly and without mathematical transformations or transfer functions [27,28]. Central pressure waves are recorded directly over the carotid artery, and are calibrated using mean and diastolic brachial pressures, a method recognized widely in the scientific literature [4,17,35,38].

Attending to the enormous potential of this new technological option, it is crucial and of greater importance to address its reliability in obtaining the carotid pressure curve, which is the main aim of this study. For this purpose, simultaneous central arterial pressure curves were obtained by heart catheterization and Complior Analyse, and the concordance between methods was analyzed. To the best of our knowledge, this is the first validation research of the new Complior device with invasive central hemodynamic data.

Methods

Study population

Fifteen consecutive patients (seven of whom were women), mean age 62.07 ± 10.59 years (ranging in age from 45 to 84 years), undergoing routine diagnostic coronary angiography at the Unidade de Intervenção Cardiovascular of the Centro Hospitalar e Universitário de Coimbra-Hospital Geral, between May and July 2013, were enrolled in a cross-sectional study aiming to validate the new Complior Analyse device (ALAM Medical, Paris, France). Patients with a history of peripheral arterial disease or large artery atherosclerotic disease, aortic aneurysm, active malignancy, hypotension [systolic blood pressure (SBP) < 90 mmHg], valvular heart disease, left ventricle dysfunction (ejection fraction < 50%), or frequent arrhythmias were excluded.

All patients participated in this study voluntarily and provided informed consent to participate.

The main characteristics of the study population are summarized in Table 1, showing a relatively overweight population (mean BMI = 26.09 ± 2.10 kg/m²), with a high prevalence of dyslipidemia (93%) and arterial hypertension (80%). Four patients (27%) had diabetes and seven patients (47%) were active smokers. In terms of coronary disease, 67% (n = 10) of the patients had a history of previous myocardial infarction, 20% (n = 3) had previously undergone coronary bypass surgery, and 60% (n = 9) had received previous percutaneous coronary interventions.

General protocol

Central pressure curves were obtained simultaneously with left cardiac catheterization and the Complior Analyse in all patients. Brachial blood pressure (BP) was measured in a supine position and after a 10-min resting period by an experienced operator and using a clinically validated (class A) sphygmomanometer (Colson MAM BP 3AA1-2; Colson, Paris, France) [39]. The mean of three measurements was used in the analysis. Brachial systolic (bSBP) and diastolic (bDBP) blood pressures were used to calculate the mean pulse pressure (bPP = bSBP – bDBP) and arterial pressure (bMAP = bDBP + 1/3bPP).

For left heart catheterization, the Seldinger technique was performed over the femoral or the radial artery (as indicated). A guide-wire was then introduced, through which a 6 F fluid-filled pigtail catheter progressed to the ascending aorta, positioned under imaging control, ~ 2 cm above the aortic valve’s ring. The catheter was then connected to a pressure transducer using an infusion system. After flushing and transducer calibration, the hemodynamic polygraph was set to a 200 mmHg/10 cm sensitivity and a 100 mm/s registry speed. The system used was a Siemens Artis Zee with an AXIOM Sensis hemodynamic recording system (Siemens AG Healthcare, Erlangen, Germany).

Aortic pressure curves were used for analysis because of the absence of clinical indications for carotid catheterization, thus making the positioning of the catheter directly in the carotid artery ethically unacceptable.

For the noninvasive carotid pressure curve registration with the Complior Analyse device, the patient’s neck was placed in slight hyperextension and was slightly rotated to the left. The Complior’s carotid probe was then positioned over the right carotid artery using the device’s specific mechanical support. The probe was adjusted until a good-quality signal was recorded in terms of stability, definition, and magnitude (point of maximum

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Table 1  General characterization of the study population (n = 15)

<table>
<thead>
<tr>
<th>Sex [n (%)]</th>
<th>Female</th>
<th>7 (47)</th>
</tr>
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<tbody>
<tr>
<td>Male</td>
<td>8 (53)</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>62.07 ± 10.59</td>
<td></td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>26.09 ± 2.10</td>
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<tr>
<td>Systolic pressure (bSBP) (mmHg)</td>
<td>145.60 ± 22.81</td>
<td></td>
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<tr>
<td>Diastolic pressure (bDBP) (mmHg)</td>
<td>72.00 ± 8.86</td>
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<tr>
<td>Mean pressure (bMAP) (mmHg)</td>
<td>96.00 ± 9.78</td>
<td></td>
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<tr>
<td>Pulse pressure (bPP) (mmHg)</td>
<td>73.87 ± 25.32</td>
<td></td>
</tr>
<tr>
<td>Heart rate (bpm)</td>
<td>60.40 ± 6.78</td>
<td></td>
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<tr>
<td>Dyslipidemia [n (%)]</td>
<td>14 (93)</td>
<td></td>
</tr>
<tr>
<td>Arterial hypertension [n (%)]</td>
<td>12 (80)</td>
<td></td>
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<tr>
<td>Diabetes [n (%)]</td>
<td>4 (27)</td>
<td></td>
</tr>
<tr>
<td>Tobacco [n (%)]</td>
<td>7 (47)</td>
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</table>
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signal amplitude). All measurements were performed by the same highly experienced operator.

At this point, the aortic (catheterization) and the carotid (Complior) pressure curves were simultaneously registered in a time frame of 15 s. The waveforms were then averaged and the mean values were extracted for the 15 s window of acquisition. The quality of the recorded pressure waves was immediately evaluated by two independent and highly experienced observers. Complior’s carotid waveforms were calibrated with bMAP, measured immediately before the simultaneous acquisition.

The pressure curves were then analyzed, and morphological and temporal components of the waveforms were extracted. For the invasive aortic curves, the MATLAB (Mathworks, Natick, Massachusetts, USA) software was used. The following central hemodynamic parameters were calculated for both methods: central SBP (cSBP), cPP, augmentation index, augmented pressure, systolic pressure amplification, pulse pressure amplification, left ventricle ejection time, and diastolic time. All of the waveform’s quantitative analyses were carried out by the same observer.

Statistical analysis

Data were computerized and treated using STATA, version 11.0 (StataCorp., College Station, Texas, USA; 2009. STATA statistical software: release 11.0).

The distribution of the variables was tested for normality using the Shapiro–Wilks test, and for homogeneity of variance by the Levene test. Simple descriptive statistics were used to characterize the sample and the distribution of variables. Data are presented as mean ±SD for continuous variables and as frequency (%) for categorical variables. Noninvasive and invasive parameters were compared using a Student’s paired t-test and Bland–Altman analysis was carried out to address the concordance between methods estimating the considered central waveform parameters. Bland–Altman plots were constructed (chart showing the relative differences between both methods in relation to its average) and correlations between measurements were determined using Pearson’s r coefficient. The intraclass correlation coefficients were determined to assess the overall strength of agreement. Differences between invasive and Complior variables were expressed as mean difference ±SD, and the corresponding confidence interval (CI), as recommended in Bland–Altman analysis [40].

A P-value of up to 0.05 was considered to indicate statistical significance, at a 95% CI.

Results

The overall strength of agreement for the central arterial pressure curve variables was very good, with intraclass correlation coefficients above 0.96, indicative of a strong concordance between the two methods (Table 2). This was further confirmed by the observation of small, positive, mean differences for central arterial pressures and other waveform components, with no significant terms in the pairwise comparisons (P > 0.1 for all variables).

The Bland–Altman analysis for cSBP and cPP (Fig. 1) also showed a strong correlation between the invasive and the noninvasive estimates, and quite small and positive mean differences (ΔcSBP = 1.80 ± 4.20 mmHg; ΔcPP = 1.67 ± 3.75 mmHg), with all individual values within the concordance limits defined by the 95% CI. Curiously, the Bland–Altman plots showed a positive bias for lower pressure values, resulting in a small overestimation of Complior’s pressure estimates for lower pressures, converting into a negative bias for higher pressure values and thus, a small underestimation for higher pressures. Nevertheless, the mean differences observed, all below 2 mmHg for the considered pressures, are indeed noteworthy.

Arterial pressure amplification was identified in both invasive and noninvasive pressure estimations (cf. Fig. 2), although the Complior was associated with a small underestimation of cSBP (Δ = −1.80 ± 4.19 mmHg) and cPP (Δ = −1.67 ± 3.75 mmHg). As an additional, but rather clinically relevant, result, we identified a strong inverse relation of pressure amplification with age, with a correlation coefficient of −0.82 for SBP amplification and −0.71 for PP amplification (Fig. 3). This relation was identified for the invasively and noninvasively determined pressure amplification, and stresses the particular relevance of this technology for younger patients.

In terms of the augmentation index, an important surrogate of reflected waves, a stable pattern of concordance between methods was found all along the variable’s continuum (cf. Fig. 4), with a quite small positive bias (Δ = 0.24 ± 0.84%) and a strong correlation (R = 0.99). Similar findings were obtained for other variables, such as the left ventricle ejection time and the diastolic time (Fig. 5).

All the correlation coefficients were independent of the clinical profile of the patients, namely, age, sex, and BMI.

Discussion

The clinical usefulness and measurement of central arterial pressures, and its growing validation as a risk marker, has been a fundamental topic of research and debate within the scientific community [2–7]. In fact, recent evidence has shown that central arterial pressures are superior in the prediction of cardiovascular events when compared with peripheral arterial pressures [2–7, 12,13]. Moreover, the evidences in favor of the central pressure curve analysis rely not only on its superior predictive capacity but also its ability to provide decisive information for therapeutic optimization. Indeed, it was
elegantly shown [11] that different pharmacologic classes may have a different impact on the central pressure curve, indicating that therapeutic orientation only on the basis of brachial arterial pressure does not contemplate the real overall hemodynamic effect, an aspect also documented in a recent study on patients with malignant arterial hypertension [14].

The increasing recognition of the central pressure curve as a clinically fundamental feature for risk stratification and clinical decision has led to the emergence of several noninvasive methodological options for this purpose. However, and despite the existing methodological studies for some of these technologies, the available evidences are not yet sufficient to support a standard method for clinical practice [9,18,31,37,41].

With this study, we intended to evaluate the reliability of the new generation of the Complior device – the Complior Analyse, comparing its noninvasive central (carotid) pressure curve analysis against the invasive hemodynamic data obtained from heart catheterization.

### Table 2  Concordance analysis for the invasive (catheterization) and noninvasive (Complior Analyse) estimates of central arterial pulse wave analysis

<table>
<thead>
<tr>
<th></th>
<th>Complior Analyse</th>
<th>Cardiac catheterization</th>
<th>Mean difference ± SD (95% CI)</th>
<th>ICC (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>cSBP (mmHg)</td>
<td>138.87 ± 22.52</td>
<td>137.07 ± 25.89</td>
<td>1.80 ± 4.20 (–0.52 to 4.12)</td>
<td>0.98 (0.96–0.99)</td>
</tr>
<tr>
<td>cPP (mmHg)</td>
<td>69.27 ± 23.21</td>
<td>67.60 ± 26.44</td>
<td>1.67 ± 3.75 (–0.41 to 3.75)</td>
<td>0.98 (0.96–0.99)</td>
</tr>
<tr>
<td>AIX (%)</td>
<td>14.64 ± 17.40</td>
<td>14.40 ± 16.94</td>
<td>0.24 ± 0.92 (–0.27 to 0.75)</td>
<td>0.99 (0.99–1.00)</td>
</tr>
<tr>
<td>AP (mmHg)</td>
<td>14.99 ± 13.73</td>
<td>14.75 ± 13.69</td>
<td>0.24 ± 0.84 (–0.26 to 0.72)</td>
<td>0.99 (0.99–0.99)</td>
</tr>
<tr>
<td>SPamp (mmHg)</td>
<td>6.80 ± 3.01</td>
<td>8.60 ± 4.30</td>
<td>–1.80 ± 4.19 (–4.10 to 0.50)</td>
<td>0.98 (0.97–0.99)</td>
</tr>
<tr>
<td>PPamp (mmHg)</td>
<td>4.41 ± 4.9</td>
<td>6.06 ± 5.28</td>
<td>–1.67 ± 3.74 (–3.74 to 0.41)</td>
<td>0.98 (0.97–0.99)</td>
</tr>
<tr>
<td>LVET (ms)</td>
<td>344.00 ± 2773</td>
<td>337.33 ± 39.55</td>
<td>0.94 ± 23.62 (–6.42 to 19.75)</td>
<td>0.99 (0.99–1.00)</td>
</tr>
<tr>
<td>DT (ms)</td>
<td>662.07 ± 89.59</td>
<td>661.33 ± 90.40</td>
<td>0.73 ± 1.67 (–0.19 to 1.66)</td>
<td>0.99 (0.99–1.00)</td>
</tr>
</tbody>
</table>

AIX, augmentation index; AP, augmented pressure; CI, confidence interval; cPP, central pulse pressure; cSBP, central systolic blood pressure; DT, diastolic time; ICC, intraclass correlation; LVET, left ventricle ejection time; PPamp, pulse pressure amplification; SPamp, systolic pressure amplification.

Bland–Altman analysis of agreement between noninvasive (Complior Analyse) and invasive (heart catheterization) central arterial pressures. Left panel: scatter plots and correlation coefficients. Right panel: Bland–Altman plots of differences between Complior and invasive values. The solid line represents the mean difference and dashed lines correspond to the mean difference ± 1.96 SD. PP, pulse pressure; SBP, systolic blood pressure.
The results showed a strong concordance in central arterial pressures, the augmentation coefficients, and the overall wave morphology. Comparison between methods showed small mean differences for all the variables analyzed, with a slight positive bias toward noninvasive estimates, probably a result of the different arterial points where hemodynamic curves were acquired—ascending aorta (invasive) versus carotid artery (noninvasive). Nonetheless, the noninvasive measurements showed an overall good reliability for all the parameters, in agreement with recent data [28] that evaluated the Complior Analyse’s pressure sensor precision, comparing it with invasive pressure curves over the radial artery. In this study [28], the noninvasive and invasive waveforms were compared in both the time and the frequency domain, and a strong correlation between methods was also found, indicating an excellent reliability of the new Complior device pressure curves over the radial artery. Another recent study [27] compared the Complior Analyse with the SphygmoCor (SCor; AtCor, West Ryde, New South Wales, Australia), also showing a good correlation between both methods. The cumulative evidences available, to which our data contribute, clearly indicate a good technical profile of this new device for central pulse wave analysis, with a quite good overall reliability and a stable performance, independent of sex, age, arterial pressure, and BMI.

An important relative advantage of the Complior Analyse over other existing methods is the possibility of simultaneously measuring aortic pulse wave velocity, allowing for a one-shot acquisition of decisive hemodynamic parameters for overall cardiovascular risk stratification and clinical decision. However, the direct measurement of central arterial pressures over the carotid artery, not relying on mathematical transfer functions, is also a key advantage, given the well-known limitations of the mathematical transformations found in much of the other devices available [32–37]. This characteristic was indeed a foremost motivation for this study, given that the nondependence of mathematical functions for transforming the central pressure curves could ensure greater accuracy when measuring the pressure curve.

Despite being technically simple, this methodology demands an adequate amount of training; thus, it should be performed by an experienced, adequately trained professional with good theoretical knowledge of arterial physiology and hemodynamics [9].

Notwithstanding the consistency of the results presented, some limitations should be considered when interpreting the data, mainly the impossibility of acquiring the pressure curves simultaneously at the carotid artery level. In fact, all of the patients had indications for cardiac catheterization, making carotid catheterization ethically unacceptable. Naturally, comparison of ascending aortic pressure curves with carotid artery ones must be considered with caution because of the hemodynamic

![Fig. 2](image-url)

Comparison of brachial arterial pressures measured noninvasively and central arterial pressures determined invasively and by the Complior Analyse. Mean and range (minimum and maximum values) of central systolic blood pressure (cSBP) and central pulse pressure (cPP) are shown.*P < 0.001. bPP, brachial pulse pressure; bSBP, brachial systolic blood pressure.

![Fig. 3](image-url)

Correlation between age and systolic blood pressure (SBP) and pulse pressure (PP) amplification.
regional differences. In contrast, retrieving pressure curves directly over the carotid artery in patients with carotid catheterization indication, and hence, with important carotid atherosclerotic disease, would limit the extrapolation of the results to populations without significant atherosclerotic disease over the same arterial segment as atherosclerotic plaques markedly affect regional hemodynamic features.
The study population, albeit small in number, was heterogeneous enough in terms of age and other clinical and anthropometric features to allow for an appreciation of this method’s reliability dependence over different physical and clinical profiles. However, the high cardiovascular risk profile of these patients advises caution when extrapolating the results to low-risk or intermediate-risk patients. Another critical point that needs consideration refers to whether these hemodynamic parameters are clinically useful to all patients. This was not the aim of the present study, but should nevertheless be considered as recommended recently [41]. The main support for central pulse wave analysis comes from the pressure amplification that hinders a rigorous and correct hemodynamic profiling on the basis of brachial pressures alone. In this sense, patients with small or no pressure amplification will not benefit from further analysis with this technologies, as in the case of older patients as our data show. In contrast, patients with marked pulse amplification will definitely benefit from central pulse wave analysis. It is then crucial to establish standard recommendations for the use of these technologies, identifying the methods to use, their relative equivalence, reference values, clinical indications, and decision-making algorithms on the basis of risk stratification and therapeutic profiling.

Conclusion
The available evidence shows that the Complior Analyse is a reliable option for the acquisition of carotid pressure curves and pulse wave analysis. Its suitability, in methodological terms, for clinical practice has thus been shown. Longitudinal studies will be necessary to assess its predictive capacity for cardiovascular events and its role in therapeutic optimization and clinical decision, although the existing data, on the basis of other methodologies, indicate quite promising and positive results.

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Conflicts of interest
There are no conflicts of interest.

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