

# Estimation of Cardiac Output from Left Ventricular Pressure by a Modified Modelflow Method

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## Abstract

*The Modelflow method (MM) requires the recording of the aortic pressure signal, to compute cardiac output (CO) by simulating a non-linear three-element model of aortic input impedance. We propose an extended MM to be applied to the intraventricular pressure signal, to obtain an independent estimation of CO in the setting of conductance measurements. Hemodynamic tests were performed in 21 patients with heart failure during atrio-biventricular pacing. Comparing CO by extended MM simulation with standard MM, the bias was -0.04 (0.36) l/min, with limits of agreement of -0.77 and 0.70 l/min, and a coefficient of variation of 8.4%. In patients without mitral and aortic abnormalities, the continuous CO estimation with the proposed method seems reliable. This method presents an acceptable precision to replace conventional aortic MM estimation in subjects undergoing intraventricular pressure acquisition, such as during conductance catheter evaluation.*

## 1. Introduction

The multielectrode conductance catheter performs continuous and accurate ventricular volume measurements with high time resolution over single cardiac cycles [1]. However the concomitant use of an independent system for cardiac output (CO) estimation is advisable to confirm the results obtained with conductance method, particularly when CO measure can be affected by artifacts [2].

A possible approach is the simultaneous use of pressure signal analysis methods such as the Modelflow. According to Wesseling et al. [3], this method derives an aortic flow waveform from arterial pressure by simulation of a non-linear three-element aortic input impedance model, estimates stroke volume (SV) by integrating the flow waveform and calculates CO by multiplying SV by

the heart rate. This method was demonstrated to reliably monitor CO changes in a wide range of hemodynamic states and to precisely estimate absolute values of CO after calibration.

The implementation of the Modelflow method requires the acquisition of the aortic pressure (Pao) signal that, during conductance measurements, can be obtained inserting a second micromanometer catheter in aorta or using a dual pressure sensor conductance catheter, which is not widely available.

In this paper, we propose to derive aortic flow waveform from the left ventricular pressure (Plv) by using a modified version of the Modelflow method, to obtain a simplified independent estimation of CO in the setting of conductance measurements.

## 2. Methods

### The model

The aortic Modelflow method (MFao) computes relative CO from Pao (CO-MFao) using a nonlinear, time-varying three-element Windkessel model [3]. The model includes aortic characteristic impedance (Z0), arterial compliance (Cw), and systemic vascular resistance (Rp) (Figure 1). Z0 and Cw depend on the aortic cross-sectional area, which can be estimated from mean arterial pressure, age, and sex by means of the arctangent model of Langewouters et al. [4]. However, these estimations are not accurate and the absolute value of the estimated CO remains uncertain, unless calibration against another method of measurement such as thermodilution is performed. For each beat, Rp is obtained as the ratio of mean Pao and the CO estimated with the previous beat. With this scheme, the model can follow changes in systemic peripheral resistance that occur with a time constant which is typically about 10s.

To permit the computation of CO from Plv signal (CO-MFlv), we extended the described model simulating the

aortic valve (Figure 1, dashed box). The first assumption of this model is the absence of systolic mitral regurgitation as the model computes forward flow into the aorta and ignores eventual backward flow. Moreover, in the hypothesis of patent aortic valve, we assumed a fixed value resistance ( $R_{ao}$ ) placed in series to  $Z_0$  during the ejection phase (Figure 1, first panel). In diastole (Figure 1, second panel) we considered the absence of leakage (infinite resistance): the absence of aortic flow and an estimated  $P_{ao}$  determined by the discharge of  $C_w$  over  $R_p$ , from the initial value recorded at the time of end-systole.

In our model the time of end-systole, that in MFao is detected at the first local minimum in the aortic flow signal after peak flow in correspondence of the dicrotic notch, is selected as the time of negative  $dP_{lv}/dt$  max, while the time of the end-diastole is determined by the crossing of the decreasing estimated  $P_{ao}$  by the simultaneously increasing  $P_{lv}$  (Figure 2).

In order to characterize the  $R_{ao}$ , instead of using an arbitrary fixed value, the following procedure is proposed. The typical approach for conductance catheter placement is the retrograde insertion via the femoral artery. Before accessing the left ventricle (LV), the  $P_{ao}$  can be recorded using the catheter micromanometer. A second acquisition is then performed with the catheter in the final location and the transducer placed in LV. Thus, the  $R_{ao}$  value can be determined as the mean difference of  $P_{lv}$  and  $P_{ao}$  during the systolic phase divided by the CO-MFao estimated from the  $P_{ao}$  recording.

Once characterized  $R_{ao}$ , its value is entered into the model and the aortic flow can be obtained simulating digitally the non-linear model. CO-MF<sub>lv</sub> is then computed by integrating the flow during systole and multiplying by heart rate.

Usually, before conductance volume acquisitions, a thermodilution CO measurement (CO<sub>td</sub>) is carried out as part of the initial calibration procedure. This result can be also applied for CO-MF<sub>lv</sub> calibration, which was shown to improve the precision of the method by reducing the uncertainty in the patient's aortic diameter and is performed by multiplying CO-MF<sub>lv</sub> by a calibration factor  $K_{lv} = CO_{td} / CO-MF_{lv}$ .

## Patients and materials

21 patients with heart failure (15 males, 10 ischemic, mean ejection fraction 27(6)), undergoing biventricular pacing device implantation for cardiac resynchronization

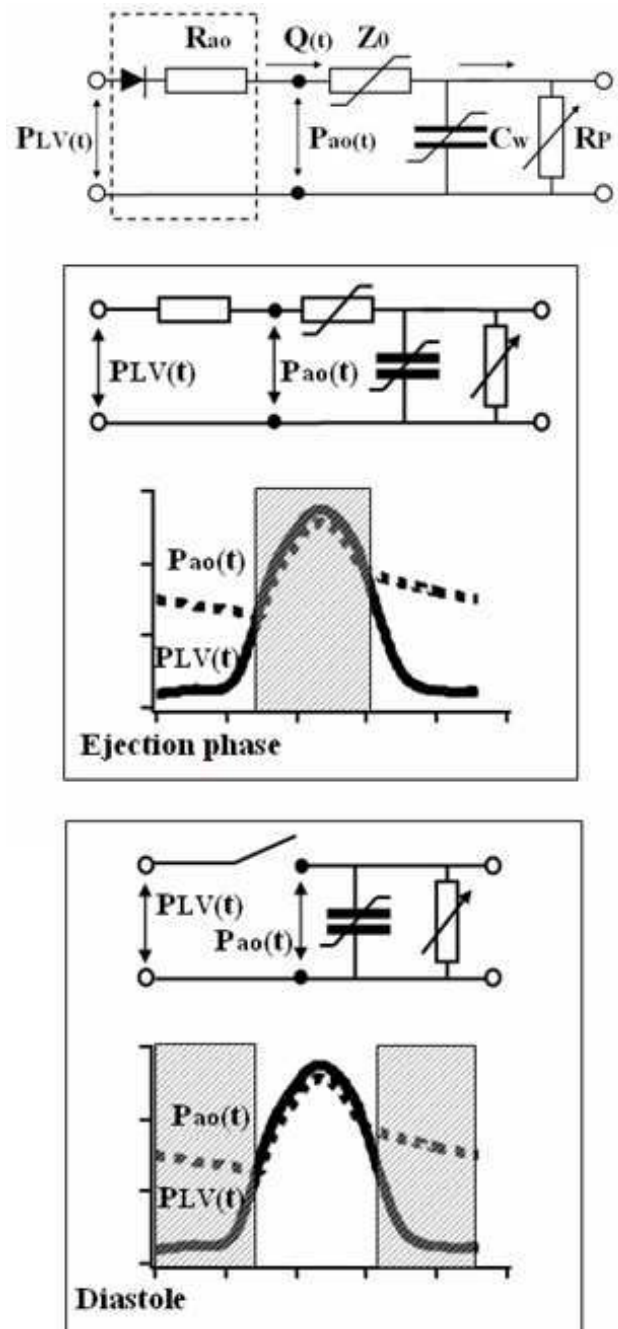


Figure 1. The standard Modelflow method uses a nonlinear, time-varying three-element Windkessel model: aortic characteristic impedance ( $Z_0$ ), arterial compliance ( $C_w$ ), systemic vascular resistance ( $R_p$ ), aortic flow ( $Q(t)$ ). To describe the aortic valve the model has been extended (dashed box). In ejection phase it includes an extra linear impedance ( $R_{ao}$ ), while in diastole  $Q(t)$  is zero: an estimated aortic pressure ( $P_{ao}$ ) is determined by the discharge of  $C_w$  over  $R_p$ , from the initial value recorded at the time of end-systole.

therapy, were studied at the time of the procedure.

After right auricular, right ventricular and LV stimulation catheters were placed, two micromanometer catheter (Millar No. SPC-474A, Millar Instruments, Houston, TX) were placed in LV and in aorta. The simulation and the data analysis were performed with a custom-made software developed in LabVIEW 5.1 (National Instruments, Houston, TX, USA).

### Measurement protocol

Hemodynamic tests were performed during temporary stimulation both in dual chamber pacing and in atrial tracking ventricular pacing. In each patient, we performed acquisitions at baseline and for each combination of different A-V (ranging from 80 ms to 160 ms, with steps of 20 ms) and V-V (from -60 ms to 40 ms, with steps of 20 ms). For each step, a 30 s recording period was preceded by a stabilization period of 30 s. All measures were averaged over 10-15 cardiac cycles after extrasystolic beats were removed from analysis. During offline analysis some recordings were discarded due to excessive arrhythmic beats. We compared CO-MFlv values with standard CO-MFao measures.

### Statistical analysis

Data averages are given as mean and standard deviation (SD). Limits of agreement were computed plotting differences in data pairs against their average (Bland-Altman plots). The agreement between the two models is computed as the bias (mean), with limits of agreement computed as bias  $\pm$  2SD when differences followed normal distribution. Normality was tested with the Kolmogorov-Smirnov one-sample test. The coefficient of variation was computed as CV = (SD/mean) $\times$ 100%.

## 3. Results

In 21 patients a total of 516 measures of acceptable quality were used for comparisons between CO-MFlv and CO-MFao.

In Figure 2 the acquired signals and the waveforms generated with the two methods are reported.

Table 1 summarizes the results obtained in our patients, the data are presented in two fashions: averaged per patient and then pooled for the group, and with all the measurements pooled.

The overall mean CO was 4.36 (1.38) l/min. Our multisite ventricular stimulation protocol produced large changes in the hemodynamic state of patients: within patients CO ranged up to 2:1 ratio during the tests, while pooling all series the range ratio for CO was 3:1.

Comparing the two Modelflow methods, the absolute error ranged from -0.27 l/min to 0.31 l/min, with a SD ranging from 0.17 l/min to 0.52 l/min. The mean absolute

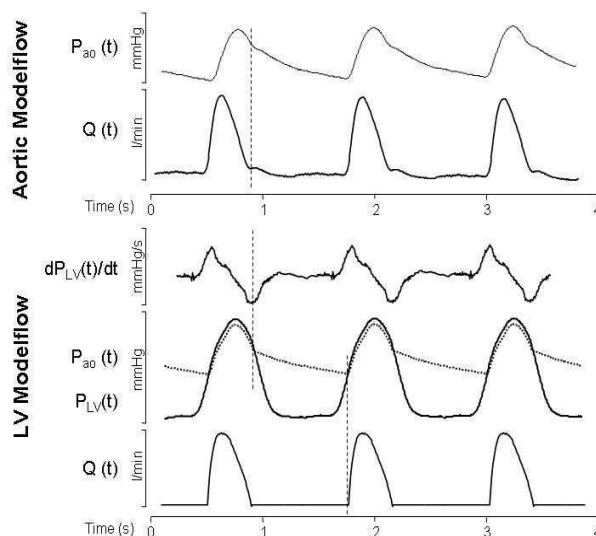


Figure 2. Acquired signals and waveforms generated with the three methods. Aortic Modelflow: acquired aortic pressure ( $P_{ao}(t)$ ) and estimated aortic flow signal ( $Q(t)$ ). The dicrotic notch is detected by identifying the first local minimum of  $Q(t)$  after peak flow. LV Modelflow: acquired LV pressure ( $P_{lv}(t)$ ) and its first derivative ( $dP_{lv}(t)/dt$ ), estimated aortic pressure ( $P_{ao}(t)$ ) and aortic flow signal ( $Q(t)$ ). The end-systolic time is identified considering the negative  $dP_{lv}/dt$  maximum, while the time when the  $P_{lv}$  signal, during its systolic increase, crosses the simulated  $P_{ao}$  signal identifies the end-diastole.

Tab 1. Cardiac output estimation with MFlv versus standard MFao.

Patient	N of Series	min CO (l/min)	max CO (l/min)	Rao (mmHg's/l)	CO-MFlv Vs CO-MFao		
					CO dif (l/min)	ED-point error (ms)	ES-point error (ms)
1	12	2.65	4.33	5.0	-0.27 (0.28)	24.9 (4.1)	43.4 (15.4)
2	20	2.77	3.43	6.6	-0.25 (0.20)	35.9 (2.9)	5.3 (3.9)
3	37	2.82	3.52	7.1	-0.03 (0.28)	28.2 (3.8)	23.8 (6.9)
4	16	2.85	3.39	4.8	0.02 (0.31)	19.2 (3.9)	25.4 (5.1)
5	41	3.25	5.78	4.6	0.00 (0.42)	91.4 (3.4)	105.9 (8.4)
6	20	4.12	4.85	4.5	-0.14 (0.33)	26.0 (2.6)	31.1 (4.4)
7	3	3.31	3.39	6.4	0.09 (0.17)	11.8 (3.7)	37.5 (1.3)
8	13	2.66	3.60	7.6	-0.20 (0.27)	36.1 (15.6)	19.0 (17.5)
9	22	2.87	5.01	7.7	0.31 (0.26)	12.8 (8.8)	22.5 (10.0)
10	23	3.82	4.85	6.7	0.31 (0.22)	37.8 (3.1)	28.6 (2.6)
11	47	5.33	7.30	5.7	-0.19 (0.47)	17.4 (4.7)	21.1 (2.6)
12	33	2.42	2.81	7.2	0.05 (0.20)	5.0 (2.9)	26.5 (2.5)
13	27	3.38	4.52	4.9	0.18 (0.20)	24.8 (2.1)	26.0 (1.8)
14	21	2.97	3.55	5.2	-0.16 (0.22)	36.7 (2.8)	39.7 (3.1)
15	38	2.73	3.59	7.4	-0.21 (0.23)	26.5 (7.4)	20.9 (7.7)
16	12	3.87	4.50	6.3	-0.17 (0.24)	55.8 (4.5)	67.2 (8.6)
17	36	3.83	7.33	8.1	-0.12 (0.43)	58.9 (2.6)	63.3 (10.3)
18	35	5.09	7.59	7.8	0.00 (0.42)	51.3 (4.9)	133.6 (35.6)
19	44	2.85	3.88	5.5	-0.09 (0.26)	87.5 (2.9)	132.3 (8.5)
20	17	3.01	3.98	8.9	0.08 (0.25)	94.6 (10.5)	137.5 (10.6)
21	20	3.35	7.51	8.3	0.16 (0.52)	38.9 (10.4)	46.4 (23.3)
patient means (SD)		3.33 (0.78)	4.70 (1.52)	6.49 (1.35)	-0.03 (0.17)	39.1 (25.8)	50.3 (41.2)
pooled means (SD)					-0.04 (0.36)	42.0 (27.6)	54.8 (45.5)

error for pooled data, i.e. bias (SD), was  $-0.04$  ( $0.36$ ) l/min, with limits of agreement of  $-0.77$  and  $0.70$  l/min, and a coefficient of variation of 8.4%. The Kolmogorov-Smirnov test for the difference between CO estimations did not indicate a significant deviation from normal distributions.

Figure 3 (panels a and b) summarizes the results obtained with pooled measures. Panel a shows scatter plot of the 516 series. Panel b shows Bland-Altman plot with the difference between CO-MFlv and CO-MFao versus their mean. The 19 largest differences, those outside the limits of agreement were recorded in 4 patients.

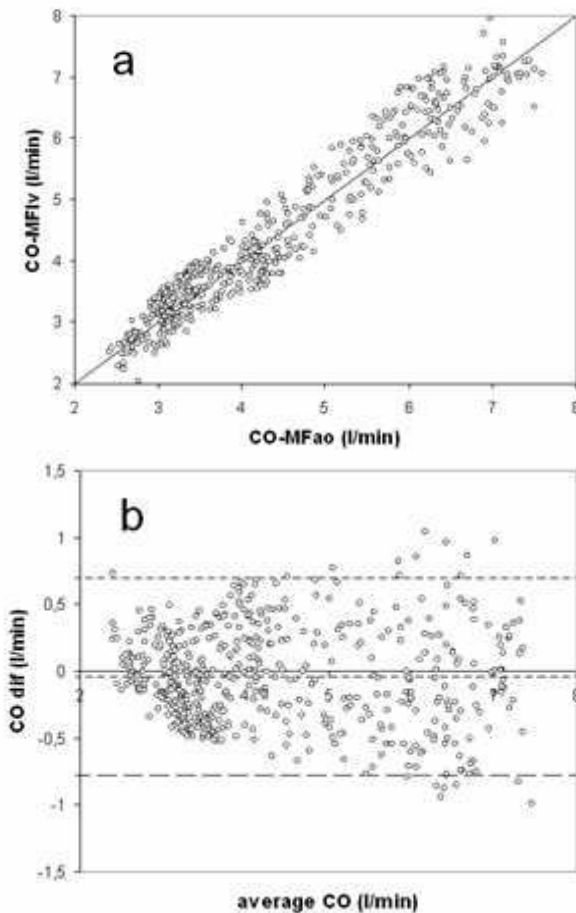


Figure 3. Diagram showing the data pairs in all 21 patients ( $n=516$ ) [Panel a]. In the Bland-Altman plot [Panel b]:  $CO_{dif} = CO_{MFlv} - CO_{MFao}$  and average CO is their mean. The dashed lines indicate the bias and limits of agreement between methods.

In MFlv method, the end-systolic point is identified by the time of negative  $dP_{lv}/dt$  max and in our tests occurred at a mean of 54.8 (45.5) ms from the dicrotic notch, as predicted by MFao (Table 2). In MFlv the end-diastolic point occurred at 42.0 (27.6) ms from the onset of the aortic flow derived from MFao. The duration of the ejection phase as estimated by MFlv resulted 12.8 (27.7) ms shorter than with MFao.

#### 4. Discussion and conclusions

Modelflow method, with Pao signal analysis, demonstrated to provide continuous precise estimations of CO. However, it requires the use of a dedicated pressure transducer in aorta.

In this study we presented a method for Modelflow computation from Plv signal. In patients without mitral and aortic abnormalities, the continuous monitoring CO using the intra-ventricular pressure signal seems reliable. CO can be monitored quantitatively and continuously with a simple and low-cost method. After an initial calibration that can be executed simultaneously and automatically during conductance calibration, this method presents near zero bias and an acceptable precision sufficient to replace conventional aortic Modelflow estimations. The measurement of CO from Plv signal can be extremely useful as an independent method during conductance catheter evaluations [2], or to permit CO estimation whenever a single pressure transducer is positioned in LV for quantifying the contractile state by measuring the  $dP_{lv}/dt$ .

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