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# Non-invasive Estimation of Right Atrial Pressure using Inferior Vena Cava Echography

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## Abstract

The pulsatility of the inferior vena cava (IVC) reflects the volume status and the central venous pressure of patients. The standard clinical indicator of IVC pulsatility is the caval index (CI), measured from ultrasound (US) recordings. However, its estimation is not standardized and prone to artefacts, mostly related to IVC movements during respiration. Thus, we used a (recently patented) semi-automated method that tracks IVC movements and averages the CI across an entire section of the vein, which provides a more stable indication of pulsatility. This algorithm was used to estimate the CI, pulsatility indicators reflecting either respiratory or cardiac stimulation and the mean diameter of IVC. These IVC indices, together with anthropometric information, were used as potential features to build an innovative model for the estimation of the right atrial pressure (RAP) recorded from 49 catheterized patients. An exhaustive search was carried out for the best

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among all possible models which could be obtained by using combinations of these features. The model with minimum estimation error (tested with a leave-one-out approach) was selected. This model estimated RAP with an error of about  $3.6\pm 2.6$  mmHg (mean $\pm$ standard deviation; whereas, the error when using only operator measured variables, without the use of the software, was about  $4.0\pm 2.5$  mmHg). These promising results underline the need for further study of our RAP estimation method on a larger dataset.

*Keywords:* Inferior Vena Cava, Ultrasound, Right Atrial Pressure, Pulsatility, Caval Index, Regression Model

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## 1 **Introduction**

2 The pulsatility of the inferior vena cava (IVC), estimated from ultra-  
3 sound (US) measurements by a non-invasive procedure, reflects the intravas-  
4 cular volume status of critical patients (Finnerty et al. (2017))(Au and Fields  
5 (2017))(Airapetian et al. (2015))(Charbonneau et al. (2014)). It has been in-  
6 vestigated in many applied studies, e.g., in cardiology patients with heart  
7 failure (Wattad et al. (2015)), pulmonary hypertension (Galié et al. (2016)),  
8 in critical patients (Akkaya et al. (2013)), in case of liver fibrosis or cirrho-  
9 sis (Kitamura and Kobayashi (2005)), in healthy blood donors (Lyon et al.  
10 (2005)) and healthy paediatric patients (Haines et al. (2012)).

11 However, the classical procedure (based on subjective measurements of  
12 the operator) is not standardized (Wallace et al. (2010))(Resnick et al. (2011))  
13 (Zhang et al. (2014)) and is affected by artefacts, like those induced by the  
14 movements of the vessel relative to the transducer during the respiratory  
15 cycle (Blehar et al. (2012)).

16 In recent works (Mesin et al. (2015))(Mesin et al. (2018)), a semi-automated  
17 method has been introduced to track the movements of the IVC in long-axis  
18 US scans in order to compensate for respiration artefacts. Tests in simu-  
19 lations indicate that the method provides a more precise estimation of the  
20 IVC local pulsatility compared to the classical measurements (Mesin et al.  
21 (2015)). Moreover, computing the vein diameters from an entire portion of  
22 the vessel (Mesin et al. (2018)) and in an orthogonal direction to the IVC  
23 midline (Pasquero et al. (2015)) allows the retrieval of overall pulsation in-  
24 formation of the considered vein portion.

25 Here, the classical and semi-automated approaches are further investi-

26 gated in terms of the possibility of extracting information on the central  
27 venous pressure (CVP). Patients with different cardiopathies were first in-  
28 vestigated using US scans and then catheterized to measure the right atrial  
29 pressure (RAP, assumed approximately equal to the CVP). Different patient  
30 characteristics (anthropometric and IVC statics and dynamic behaviour, esti-  
31 mated either using the classical or the semi-automated approach) were used  
32 to build regression models for the RAP estimation. Those with minimum  
33 error were selected.

## 34 **Materials and Methods**

### 35 *Automated detection of the IVC borders*

36 The algorithm proposed in (Mesin et al. (2018)) was used to process US  
37 video-clips. In brief, the algorithm (implemented in MATLAB R2018a, The  
38 Mathworks, Natick, Massachusetts, USA) processes each frame of an US  
39 B-mode video-clip of a longitudinal view of the IVC. A continuous measure-  
40 ment of the diameters along a whole portion of the IVC is computed after  
41 compensating for possible IVC movements.

42 In the first frame of the clip, the user indicates the location of the vein,  
43 two reference points (which are then tracked to estimate IVC movements and  
44 deformations), the most proximal and distal lines to be considered and the  
45 location of the borders of the vein along the most proximal line. The software  
46 then uniformly distributes a number of lines between the most proximal  
47 and distal borders indicated by the user. The borders of the vein are then  
48 automatically detected along all these lines. Their location and direction are  
49 updated for each frame depending on the movements of the reference points.

50 The most proximal and distal lines were selected trying to include the  
 51 entire vein portion that was visualized for the whole video-clip. In optimal  
 52 conditions, the available tract was between the confluence of the hepatic veins  
 53 into the IVC and the caudate lobe of the liver. However, for most patients,  
 54 the available portion of the vein was smaller.

55 Once the superior and inferior borders of the vein (in the tract under  
 56 investigation) have been obtained, the software computes the IVC midline.  
 57 This is defined as the mean curve between the two borders. The curvilinear  
 58 abscissa is then computed along the midline. Five points are then uniformly  
 59 distributed along this line (i.e., with the same curvilinear distances between  
 60 neighboring points), considering its extension from the 20% point to the  
 61 80% point of its length (the edges of the tract were excluded). Then, the  
 62 orthogonal sections, in respect to the IVC midline, passing from each of the  
 63 5 points are considered and the pulsatility of the IVC is estimated for each  
 64 of them in terms of the caval index (CI)

$$CI = \frac{\max_t(D(t)) - \min_t(D(t))}{\max_t(D(t))} \quad (1)$$

65 where  $D$  is the estimated diameter series over the time variable  $t$  (in a specific  
 66 section) and max/min indicate local extrema. Local maxima and minima  
 67 are computed for each respiration cycle. Averaging across different cycles, a  
 68 stable estimation of pulsatility is computed for each section. Finally, a CI  
 69 accounting for the overall pulsatility of the considered portion of the vein can  
 70 be obtained by averaging the estimates across different sections (see (Mesin  
 71 et al. (2018)) for details).

72 The following additional pulsatility indices (RCI and CCI) were also es-  
 73 timated. The vein dynamics were considered as resulting from two different

74 stimulations, induced by either respiration or heartbeats, respectively. The  
75 effect of respiration was computed by low pass filtering the whole diameter  
76 time series with a cut-off frequency of 0.4 Hz. The cardiac contribution was  
77 obtained by high pass filtering the whole diameter time series with a cut-off  
78 frequency of 0.8 Hz (both filters were 4<sup>th</sup> order Butterworth; they were used  
79 twice, once with time reversed, in order to remove phase distortion and de-  
80 lay). From the two filtered time series, applying again the definition of CI  
81 given in (1), the respiratory caval index (RCI) and the cardiac caval index  
82 (CCI) were obtained.

### 83 *Experimental data*

84 The study was approved by the Ethics Committee of the University Hos-  
85 pital of Trieste and complies with the principles of the Declaration of Helsinki.  
86 Informed consents were obtained from the patients participating in the study.

87 We prospectively enrolled 62 patients (consecutively from 1/12/2015 to  
88 1/9/2017) undergoing echocardiographic assessment and right heart catheter-  
89 ization (RHC) for all clinical indications. Some of them were excluded, for  
90 the following technical problems: IVC not visible (due to either abdominal  
91 gas, excessive fat tissue, low definition of the edges of the vein) and paradox-  
92 ical IVC movements (distal collapse and proximal dilatation or vice versa).  
93 Finally, 49 patients with good US scans (i.e., allowing reliable processing)  
94 could be included in the study (26 males and 23 females; mean±standard  
95 deviation - STD: age 62.2±15.2 years, weight 71.7±15.3 kg, height 168.1±9.3  
96 cm). The selected patients had the following pathologies: 28 patients (57%)  
97 were affected by various heart disease (hypertensive, ischemic, valvular, toxic  
98 and tachy-induced cardiomyopathy), 10 patients (20.4%) had hypertrophic,

99 dilated or restrictive cardiomyopathy and 11 patients (22.5%) showed non  
100 group 2 pulmonary hypertension. The following machines were used to record  
101 the US video-clips: VIVID E9, VIVID I and VIVID Q, by General Electric  
102 (Wauwatosa, WI USA); iU22, by Philips (Bothell, WA USA). A scan of at  
103 least 5 seconds of the IVC in the longitudinal axis was performed by B-Mode  
104 echocardiography during at rest breathing with sub-costal approach. Clas-  
105 sical estimation of CI was obtained by measuring subjectively maximal and  
106 minimal diameters (we refer to it as the "manual" estimation).

107 *Multi-parameter model*

The following 5 features were recorded from each patient: age, height, weight, body surface area (BSA) and sex. Moreover, further parameters were extracted from US scans using either the manual or the semi-automated approach. Specifically, via the manual approach, we measured the mean diameter and the caval index, here called  $CI_{manual}$  to distinguish it from that obtained by the semi-automated method. In this way, 7 features were considered, i.e., the general 5 features listed above plus these last 2 features. Using the semi-automated approach, we computed the mean diameter (averaging across different respiration cycles and the 5 sections) and 3 pulsatility indices, i.e., CI, RCI and CCI (thus the semi-automated approach considered 9 features, i.e., the 5 general features listed above plus these 4 features). An inverse relation was assumed between the central pressure and the caval indices. A number was also added to the denominator in order to avoid division by zero and maximize the correlation between the measured RAP and the pulsatility indices. Thus, instead of using  $CI_{manual}$ , CI, RCI, CCI as features,

we used

$$\frac{1}{CI_{manual} + a_0}, \frac{1}{CI + a_1}, \frac{1}{RCI + a_2}, \frac{1}{CCI + a_3}$$

108 respectively, where  $a_0=0.7$ ,  $a_1=2.4$ ,  $a_2=0.8$ ,  $a_3=0.3$ .

109 The information contained in the features was used to estimate the RAP.  
110 The full dataset was split into training and test sets with a leave-one-out ap-  
111 proach (Theodoridis and Koutroumbas (2008)). The training set was further  
112 split into two parts: 75% to train the models and 25% to validate them. Fifty  
113 random selections of training and validation sets were considered in order to  
114 get a robust selection of the best model.

115 Based on the training set, linear regression was used to map the input  
116 features into the RAP. Two different cases were considered, including only  
117 features measurable by either the manual or the semi-automated approaches.  
118 All combinations of features were considered as inputs to build different re-  
119 gression functions (comprehensive search): all possible choices of a single  
120 feature, all pairs, triplets, ... until using all the features. Considering maps  
121 with the same number of input features, the one providing the best gener-  
122 alization to the validation sets (i.e., minimum mean estimation error on the  
123 validation sets) was then selected as optimal and applied to the test data.  
124 The optimal model was almost always the same.

125 The performances of the regression models were evaluated by considering  
126 the mean of the absolute value of the errors on the test set

$$E = |x_r - x_m| \tag{2}$$

127 where  $x_r$  and  $x_m$  are the outputs of the multivariate regression model and  
128 the measured RAP, respectively. Moreover, the standard deviation and kur-  
129 tosis of the estimation error were computed. The mean value and standard

130 deviation of errors quantify the accuracy of the estimation, while the kurtosis  
131 focuses on the tails of the error distribution and it measures large, spurious  
132 errors.

133 To choose the optimal dimension of the model, the one with best perfor-  
134 mances on the test set was selected.

## 135 Results

136 Table 1 provides some general anthropometric and clinical information  
137 on the patients. Table 2 reports catheterization and echocardiographic data,  
138 as well as some information on the video processing by the semi-automated  
139 algorithm.

140 Figure 1 and Table 3 show the variables recorded from the patients used  
141 to build the models for the estimation of RAP. Their relation with RAP is  
142 shown. Notice that most anthropometric indices have a low correlation with  
143 RAP. On the other hand, some relation is found between RAP and the fea-  
144 tures extracted from the IVC. For example, the index with most correlation  
145 with the RAP is IVC mean diameter (both when measured manually and  
146 automatically, but with more correlation in the latter case). In addition, the  
147 pulsatility indices show a good inverse correlation with RAP (again, more  
148 correlation is found considering the automated estimation). Other IVC size  
149 and pulsatility indices show some correlation with RAP (but were not shown  
150 in Figure 1 and Table 3): for the minimum diameter, the correlations were  
151 55.3 and 67.4%, for the maximum diameter 54.9 and 59.0%, for the manual  
152 and semi-automated methods, respectively; for  $1/(RCI + a_2)$  the correlation  
153 was 57.5%, for  $1/(CCI + a_3)$  it was 61.1%.

154 Figure 2 shows the best estimation models. In both cases, the low dimen-  
 155 sional models provided better generalization to the test set (so that overfit-  
 156 ting was found as the model included many variables). Specifically, the best  
 157 model when using the manual approach uses only one feature to fit RAP:

$$RAP_{est}^{Manual} = 0.55D_m \quad (3)$$

158 where  $D_m$  is the mean diameter measured in mm. This model suggests a  
 159 direct proportionality between the central pressure and IVC diameter. The  
 160 mean absolute error of this model is 4.04 mmHg (STD equal to 4.79 mmHg,  
 161 kurtosis 1.94). Considering two variables, the best model is

$$RAP_{est}^{Manual} = 0.52 D_m + 0.0085 age \quad (4)$$

162 where  $age$  is the age of the patient measured in years (mean absolute error  
 163 4.14 mmHg, STD 4.87 mmHg, kurtosis 1.89). This second model selected  
 164 again the mean diameter of the IVC and added a correction term due to the  
 165 age. Notice that a pulsatility index is not chosen to be included in the best  
 166 models, even if Figure 1 and Table 3 show that  $CI_{manual}$  has a high inverse  
 167 correlation with RAP. Indeed, the manually estimated caval index and diam-  
 168 eter are quite redundant (the correlation between the measured diameter and  
 169  $1/(CI_{manual} + a_0)$  is equal to 48%), so that the additional information pro-  
 170 vided by the measured IVC pulsatility was not relevant enough to contribute  
 171 to a reduction of the estimation error.

172 The best model when using the semi-automated approach uses the 2  
 173 features which are most correlated with RAP, reflecting the size of the vein  
 174 and its pulsatility:

$$RAP_{est} = \frac{4.13}{CI + a_1} + 0.52 D_m \quad (5)$$

175 It has a mean absolute error of 3.64 mmHg on the test set (STD equal to  
 176 4.48 mmHg, kurtosis equal to 2.09). The best models using either 1 or 3  
 177 features are given by the following expressions

$$RAP_{est} = 0.60 D_m \quad (6)$$

178

$$RAP_{est} = \frac{3.98}{CI + a_1} + 0.52 D_m + 0.0008 age \quad (7)$$

179 and have a mean estimation error of 3.78 and 3.71 mmHg, with STD of the  
 180 error equal to 4.53 and 4.55 and kurtosis of 2.02 and 2.03, respectively. Notice  
 181 that these 3 models are built upon the same predictors. The mean diameter  
 182 is the main feature (it is also the index with the highest correlation with RAP  
 183 among the considered features, as shown in Figure 1). CI is used to fit the  
 184 data better, by adding a slight modification to the model with a single feature  
 185 (indeed, the coefficient multiplying the diameter is reduced when comparing  
 186 the models with either 1 or 2 predictors and the additional term  $1/(CI + a_1)$ ,  
 187 directly correlated with RAP, is multiplied by a positive coefficient). Finally,  
 188 the best model using three features, in addition to the previous information  
 189 on IVC size and pulsatility, includes age (with a positive contribution, i.e., a  
 190 larger RAP is obtained for older patients, as also indicated by the positive  
 191 correlation shown in Figure 1. Notice, when comparing this model with the  
 192 one with two indices, that the contribution of IVC diameter is unaltered and  
 193 only the coefficient multiplying the pulsatility term is varied, i.e., slightly  
 194 decreased to add the contribution of age).

195 The Bland-Altman plots shown in Figure 2 (considering the best manual  
 196 and semi-automated models) indicate that the range of estimation error is  
 197 between  $\pm 10$  mmHg, but for more than 65% of tests the estimation error was

198 lower than 5 mmHg. For both models, there is a bias, as the errors are mainly  
199 positive and negative for low and large values of RAP, respectively, indicat-  
200 ing an average underestimation of the variations of RAP among different  
201 patients. However, this bias is lower for the model based on semi-automated  
202 estimation of features (slope of interpolation line equal to 0.75 and 0.53 for  
203 the manual and semi-automated models, respectively).

## 204 **Discussion**

205 Estimating RAP from US scans is a difficult inverse problem. Some rela-  
206 tion between size and pulsatility of IVC and the pressure in the right atrium  
207 has been suggested in the literature and collected into guidelines (Lang et al.  
208 (2015))(Rudski et al. (2010)). However, the lack of standardization of the  
209 procedure meant some doubts have arisen on the reliability of the estimates  
210 (Magnino et al. (2017)). Recent developments have allowed more accurate  
211 and repeatable estimation of the dynamics of the IVC, due to the tracking  
212 of the vein (Mesin et al. (2015)) and to the average of information from an  
213 entire tract of the vessel (Mesin et al. (2018)) provided by an innovative  
214 semi-automated algorithm.

215 This work shows that, in line with (Magnino et al. (2017)), IVC pulsatility  
216 investigated with the classical procedure does not provide stable information  
217 on RAP. However, the information extracted by the innovative algorithm can  
218 be profitably used to get an estimation of RAP that showed an average error  
219 of about 3.6 mmHg.

220 A limitation of our study is that the method was tested on a small  
221 database, as processing was successful only for 49 out of 62 patients. Future

222 developments will include the engineering of the software in a US system,  
223 so that the original data could be directly processed and a real time render-  
224 ing could guide the operators in order to acquire video-clips for which the  
225 processing is feasible.

226 Some properties of the patients were not available, but they could af-  
227 fect the estimation of the RAP. For example, IVC pulsatility also depends  
228 on the volume status of the subject (which could be in part investigated  
229 by bioimpedance analysis), compliance of the vein and interaction with sur-  
230 rounding tissues. Some information could also possibly be extracted from  
231 short axis scans of the vein (Folino et al. (2017)).

232 Thus, there is room to improve the estimation model, by extending the  
233 dataset, updating the processing algorithm (by integrating it with the ac-  
234 quisition of the US scan) and including more information on the patients.  
235 However, the preliminary results are promising and indicate that the semi-  
236 automated processing (including IVC movement tracking and the investiga-  
237 tion of an entire portion of the vessel) is useful for better characterization of  
238 IVC pulsatility and its relation with RAP.

239 An instrument implementing the algorithm described in this paper was re-  
240 cently patented by the Politecnico di Torino and Università di Torino (patent  
241 number 102017000006088).

## 242 **Conclusions**

243 A new promising technique has been introduced for the estimation of  
244 RAP. Higher accuracy is obtained when using a semi-automated method for  
245 the tracking and assessment of IVC pulsatility in an entire portion of the

246 vessel, than by considering manual subjective measurements (in the latter  
247 case, IVC pulsatility did not improve accuracy of RAP estimation).

248     The non-invasive assessment of RAP could have an active role in the man-  
249 agement of patients. The new tool which has been proposed, if validated in  
250 further studies, could have an important role in a variety of clinical settings.

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330 **Figure Captions**

331 **Figure 1:** Different variables versus right atrial pressure (RAP), with indi-  
332 cation of the correlation.

333 **Figure 2:** Performances of the best models for the estimation of RAP when  
334 using indices estimated with the standard (manual) or semi-automated  
335 approach. Bland-Altman plots show the difference between estimated  
336 and correct RAP versus their mean.

<b>General Data</b>	<b>Mean <math>\pm</math> STD</b>
Systolic Blood Pressure (mmHg)	115.9 $\pm$ 21.1
Diastolic Blood Pressure (mmHg)	71.3 $\pm$ 9.8
Heart Rate (bpm)	75.4 $\pm$ 15.5
Smokers	6 (12.2%)
Essential Hypertension	31 (63.3%)
Dyslipidemia	10 (20.4%)
Diabetes	14 (28.6%)
Atrial Fibrillation	14 (28.6%)
COPD	4 (8.2%)
CKD	14 (28.6%)
Cardiomyopathy (HCM, DCM, RCM)	10 (20.4%)
Non Group 2 Pulmonary Hypertension	11 (22.5%)
MHD	28 (57.1%)

Table 1: Main features of the population (COPD: Chronic Obstructive Pulmonary Disease; CKD: Chronic Kidney Disease; HCM: Hypertrophic Cardiomyopathy; DCM: Idiopathic Dilated Cardiomyopathy; RCM: Restrictive Cardiomyopathy; MHD: Multifactorial Heart Disease, i.e., hypertensive, ischemic, valvular, tachy-induced, toxic).

<b>Right heart catheterization data</b>	<b>Mean <math>\pm</math> STD</b>
$\Delta$ Echo-Cath Time (min)	213 $\pm$ 122
Mean Pulmonary Artery Pressure (mmHg)	33.4 $\pm$ 11.6
Right Atrial Pressure (mmHg)	10 $\pm$ 5.6
<b>Echocardiographic data</b>	<b>Mean <math>\pm</math> STD</b>
LV Ejection Fraction (%)	48.2 $\pm$ 19.7
Tricuspid Annular Plane Systolic Excursion (mm)	17 $\pm$ 4.7
RV FAC (%)	35.6 $\pm$ 12.8
Tricuspid E/E	5.6 $\pm$ 2.9
Tricuspid E/A ratio	1.2 $\pm$ 0.4
Expiratory IVC diameter (mm)	20.4 $\pm$ 5.5
Inspiratory IVC diameter (mm)	14.0 $\pm$ 6.5
IVC Collapsibility Index	0.35 $\pm$ 0.2
Measured Right Atrial Pressure (mmHg)	12.5 $\pm$ 7.4
Pulmonary Artery Systolic Pressure (mmHg)	53.0 $\pm$ 19.1
<b>Video Processing</b>	<b>Mean <math>\pm</math> STD</b>
Length of processed IVC tract (cm)	44.5 $\pm$ 12.3
Duration of US video clips (s)	9.3 $\pm$ 4.6
Identified respiration cycles	2.5 $\pm$ 1.3
Identified heartbeats	13.8 $\pm$ 7.5

Table 2: Echocardiographic and catheterization data (LV: Left Ventricle; RV: Right Ventricle; FAC: Fractional Area Change; IVC: Inferior Vena Cava).

<b>Variable</b>	<b>Mean <math>\pm</math> STD</b>	<b>CC with RAP</b>
Age (years)	62.2 $\pm$ 15.2	15.9%
Height (cm)	168.1 $\pm$ 9.3	5.8%
Weight (kg)	71.8 $\pm$ 15.3	14.9%
BSA (m <sup>2</sup> )	1.81 $\pm$ 0.22	12.8%
Sex	23 females/26 males	4.2%
IVC mean diameter (manual estimation)	18.6 $\pm$ 5.7 mm	56.7%
IVC mean diameter (semi-automated estimation)	15.9 $\pm$ 6.9 mm	64.6%
CI (manual estimation)	28.7 $\pm$ 16.0 %	-43.5%
CI (semi-automated estimation)	36.7 $\pm$ 23.2 %	-62.9%
RCI	20.7 $\pm$ 23.6 %	-55.4%
CCI	20.5 $\pm$ 22.9 %	-56.0%

Table 3: Variables used as features for the estimation models and their correlation coefficients (CC) with RAP (BSA: Body Surface Area; IVC: Inferior Vena Cava; CI: Caval Index; RCI: Respiratory Caval Index; CCI Cardiac Caval Index).