Threshold Sensitivity in Time Domain BRS Estimation: Minimum Beat-to-Beat Changes and Minimum Correlation

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Abstract

In the sequences technique, baroreflex sensitivity (BRS) is estimated as the slope between SBP and RR values in baroreflex sequences (BS). For BS identification, thresholds are applied to SBP and RR series and no recommendation on the appropriate values is given in the literature. Changes in their values can modify the number of BSs and the BRS estimate, making difficult to compare results from different studies, if not impossible.

In this work, optimum thresholds values for the identification of baroreflex related events are given. The results in the EuroBaVar dataset indicate that BRS analysis can be improved if no minimum SBP and RR beat-to-beat changes are imposed and the minimum SBP–RR correlation is 0.8. This combination duplicates the number of beats (located in more and longer segments) with global SBP–RR correlation close to 0.8, without introducing substantial changes in BRS estimates distribution. Also, it makes possible to estimate the BRS when BSs are not identified.

1. Introduction

The sequences technique is the most used time domain method for arterial baroreflex sensitivity (BRS) estimation. It is based in the joint analysis of SBP and RR beat-to-beat spontaneous variability, being the BRS estimated as the slope between SBP and RR values in baroreflex sequences (BS) [1]. For BS identification it is usual to impose several numerical thresholds on SBP and RR series. Such thresholds are usually set to increase the reliability of BS being a baroreflex related segment and, therefore, increase the assurance that the BRS estimate is measuring a real baroreflex effect. However their use may also reduce the ability of providing an individual estimate, particularly if the thresholds values are very restrictive and/or the analyzed subject has poor BRS function (cases associated with few or nonexistent BSs and lower BRS values).

The sequences technique was originally described in cats [1] and has been widely applied unchanged in humans, without the evidence that the thresholds values used in cats are adequate in human BRS studies. Moreover, no consensual opinion about those values is found in the literature [2, 3]. A slight modification in the thresholds values can change the number of BSs and the BRS estimate. Therefore, literature results on BRS may not be comparable in practice and the need to establish reference values is evident. In this work, the effect of changing the thresholds values for baroreflex related segments identification is studied towards the goal of establish reference values.

2. Time domain BRS estimation

Time domain BRS analysis is based on BSs identification following the BRS estimation as the slope between the corresponding SBP and RR values.

A valid BS_k, $k = 1, 2, \cdots, K$ is a SBP–RR segment with $N_k \geq N_{min}$ beats length that satisfies minimum SBP and RR beat-to-beat changes in the same direction ($\Delta_k^{\text{SBP}} \geq \Delta_{min}^{\text{SBP}}$ and $\Delta_k^{\text{RR}} \geq \Delta_{min}^{\text{RR}}$) and a minimum SBP–RR correlation value ($r_k \geq r_{min}$). Table 1 resumes the values imposed in this work for the identification of a valid BS.

Table 1. Thresholds values for BS identification.

Thresholds (Units)	BS
N_{min} (beats)	3
$\Delta_{min}^{\text{SBP}}$ (mmHg)	1
Δ_{min}^{RR} (ms)	5
r_{min} (no units)	0.8

The choice of $\Delta_{min}^{\text{SBP}}$ and Δ_{min}^{RR} values can restrict the estimated slope to values above the ratio $\Delta_{min}^{\text{RR}}/\Delta_{min}^{\text{SBP}}$. In subjects with BRS values $>$ 10 ms/mmHg, the generally accepted threshold of $\Delta_{min}^{\text{SBP}}$=1 mmHg will lead, in average, to RR values higher than 10 ms, exceeding the Δ_{min}^{RR}

range found in the literature (from 0 up to 6 ms). In poor BRS cases, there is a much smaller increase in RR for a given increase in SBP and the estimated slope is expected to be lower (sometimes < 0.5 ms/mmHg). If $\Delta^{RR}_{min}/\Delta^{SBP}_{min}$ is higher than the *true* slope, these thresholds will reject all segments and the BRS can not be quantified. It is also possible that the thresholds identify spurious segments which will lead to higher BRS estimates. These BSs with high slopes are unusual in subjects with low BRS and may not correspond to real baroreflex effects.

The r_{min} threshold value is set to specify for which value the SBP–RR correlation is considered as significant. If r_{min} is high it is expected to find less and shorter BSs. On the contrary, if r_{min} is low a higher number of beats is found at the expense of a higher SBP–RR joint variability.

After BS identification, the BRS can be estimated using the *local*, *global* or *total* approach, as detailed elsewhere [1, 4]. Figure 1 presents an illustrative example of the application of the methods. In the local approach (or Sequences technique), a slope is estimated for each BS and the mean of the slopes is the overall estimator $\mathcal{B}_{L,O}$ [1]. In the global approach, a global slope $\mathcal{B}_{G,O}$ is estimated by OLS minimization from the SBP and RR values in the set of all BSs, after local mean detrending (respectively, $\mathbf{d}_{SBP}$ and $\mathbf{d}_{RR}$) [4]. In the total approach, a global slope $\mathcal{B}_{G,T}$ is estimated by TLS minimization from the SBP and RR values in the set of all BSs, after local mean detrending and outlier BS removal (respectively, $\mathbf{d}_{SBP,\alpha}$ and $\mathbf{d}_{RR,\alpha}$) [4].

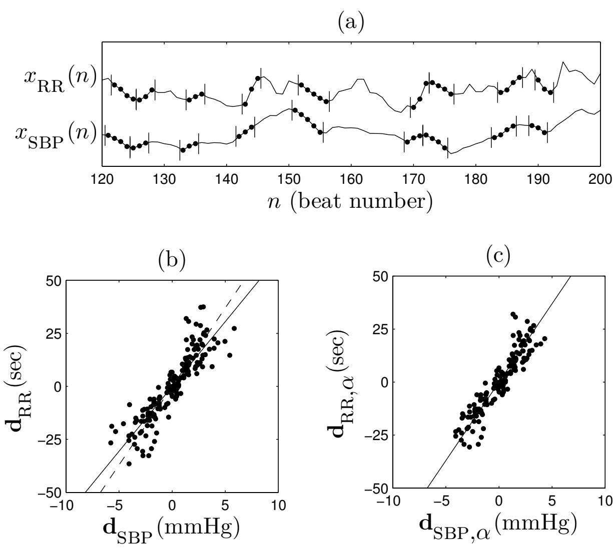

Figure 1. Illustrative example of time domain BRS estimation using the first 512 beats of the "A001LB" file from EuroBavar dataset [2]. (a) Excerpt of $x_{SBP}(n)$ and $x_{RR}(n)$ displaying with bullets the identified BS. Dispersion diagrams superimposing lines with slopes estimated by (b) local/global (dashed/full) and (c) total approach.

3. Results

The effect of changing the thresholds values in BS identification is illustrated with the 46 records of the EuroBaVar dataset [2]. In this study, the variables in table 2 were evaluated in the first 512 beats of each record considering 1 beat lag, i.e., each SBP value is paired with the subsequent RR interval. The variable r quantifies the global SBP–RR correlation, ie, the correlation between the $\mathbf{d}_{SBP}$ and $\mathbf{d}_{RR}$ variables. High values of r indicate high similarity between the slopes of all identified segments (stationarity on baroreflex sensitivity strength) while low values indicate BRS variation over time.

Table 2. BRS analysis variables (VAR) for each record.

VAR	Units	Description	Range
N	beats	# beats	[0, 512]
K	segments	# segments	[0, 128]
r	no units	$\mathbf{d}_{SBP} - \mathbf{d}_{RR}$ correlation	[0, 1]
$\hat{\mathcal{B}}_{L,O}$	ms/mmHg	local BRS estimate	[0, 30]
$\hat{\mathcal{B}}_{G,O}$	ms/mmHg	global BRS estimate	[0, 30]
$\hat{\mathcal{B}}_{G,T}$	ms/mmHg	total BRS estimate	[0, 30]

Figure 2 presents the distribution of the variables in Table 2 as a function of Δ^{SBP}_{min} and Δ^{RR}_{min}. As illustrated in column (a), when r_{min}=0.8 is imposed N<200 and K<50. The similar pattern of colors in N and K distributions indicate that the segments median length N/K is fairly constant, lower than 4 beats per segment (ratio of N and K maximum values). Probably due to the fact that N and N/K are small, r is higher than 0.8. Regarding the BRS estimates, lower Δ^{SBP}_{min} and higher Δ^{RR}_{min} values lead to higher $\hat{\mathcal{B}}$ values whereas higher Δ^{SBP}_{min} and lower Δ^{RR}_{min} values lead to lower $\hat{\mathcal{B}}$. The $\hat{\mathcal{B}}_{L,O}$ values are higher than the $\hat{\mathcal{B}}_{G,O}$ values and correlated (evidenced by a darker similar pattern of colors). For Δ^{SBP}_{min} or Δ^{RR}_{min} around zero, the $\hat{\mathcal{B}}_{G,T}$ median values present more variability due to the fact that x_{SBP} and x_{RR} in the identified segments present lower correlation. As illustrated in Figures 2(b), for Δ^{SBP}_{min}>0 or Δ^{RR}_{min}>0, the distribution of N, K, r and $\hat{\mathcal{B}}$ medians is the same either with or without r_{min}. The identified segments are the same, meaning that the corresponding x_{SBP} and x_{RR} values present correlation exceeding r_{min}=0.8. For lower Δ^{SBP}_{min} and Δ^{RR}_{min}, N increases and K decreases so that N/K increases. The value of r decreases almost to 0, because r_{min} is not imposed and also because Δ^{SBP}_{min} and Δ^{RR}_{min} are so low that almost all x_{SBP} and x_{RR} values are accepted. The $\hat{\mathcal{B}}$ values tend to 0, indicating once more no linear relation between the identified x_{SBP}–x_{RR} values. In this situation, r_{min} threshold is essential to achieve acceptable r values, in order to the linear model to be adequate.

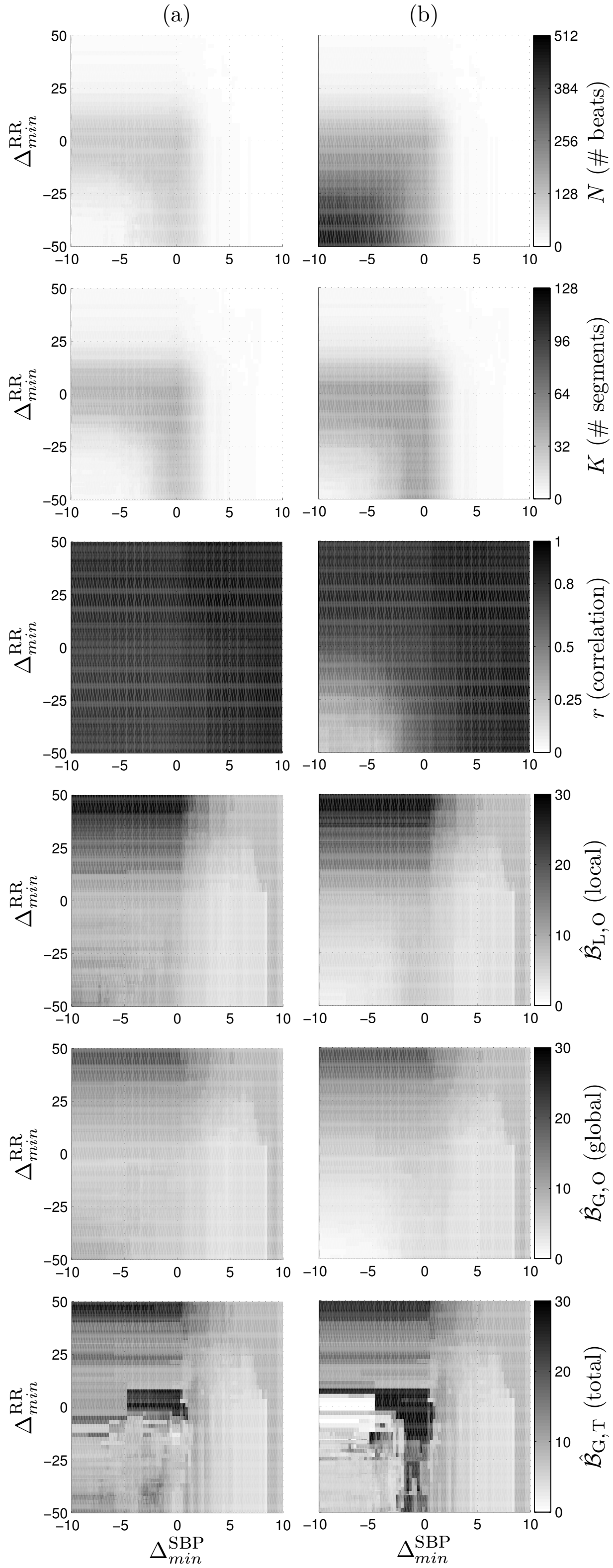

Figure 2. N, K, r and $\hat{\mathcal{B}}$ median values distribution as a function of $\Delta_{min}^{\mathrm{SBP}}$ and $\Delta_{min}^{\mathrm{RR}}$, either (a) setting $r_{min} = 0.8$ or (b) removing r_{min}. Darker indicates higher density.

Figure 3 presents the distribution of the variables in Table 2 as a function of r_{min}. As illustrated in figures 3(a), if $\Delta_{min}^{\mathrm{SBP}}$=1 and $\Delta_{min}^{\mathrm{RR}}$=5 all variables are constant for r_{min}<0.8. The identified segments are the same, meaning that the corresponding x_{SBP} and x_{RR} values present correlation exceeding 0.8. In median, N is approximately 128 of all 512 beats and K is close to 32, so that N/K is lower than 4 beats per segment. The r value is very high probably due to the small N and N/K values. For r_{min}>0.8, N and K decrease so that N/K is kept constant for all r_{min} values. The segments that exhibit lower correlation are rejected for r_{min}>0.8, leading to higher r values. As illustrated in Figures 3(b), without $\Delta_{min}^{\mathrm{SBP}}$ and $\Delta_{min}^{\mathrm{RR}}$ thresholds, N decreases and K increases for increasing r_{min}, indicating that the segments tend to be shorter in duration. The r value is close to r_{min} for 0.2<r_{min}<0.8 and around 0.8 for r_{min}>0.8. The BRS estimates $\hat{\mathcal{B}}_{\mathrm{L,O}}$ and $\hat{\mathcal{B}}_{\mathrm{G,O}}$ increase with increasing r_{min}. For small values of r_{min}, segments presenting lower x_{SBP}–x_{RR} correlation/slope are identified. When r_{min} increases, these segments are more unlikely to be identified and $\hat{\mathcal{B}}_{\mathrm{G,O}}$ tend to be more similar to $\hat{\mathcal{B}}_{\mathrm{G,O}}$ obtained when $\Delta_{min}^{\mathrm{SBP}}$ and $\Delta_{min}^{\mathrm{RR}}$ are imposed. The robust estimates $\hat{\mathcal{B}}_{\mathrm{G,T}}$ do not seem to be much affected by r_{min}, mainly due to the outlier rejection rule.

The comparison between Figures 3(a) and 3(b), evidence that without $\Delta_{min}^{\mathrm{SBP}}$ and $\Delta_{min}^{\mathrm{RR}}$ thresholds N is always higher, K is higher (for r_{min}>0.5) and r is always lower. Regarding the BRS estimates, $\hat{\mathcal{B}}_{\mathrm{L,O}}$ is higher than $\hat{\mathcal{B}}_{\mathrm{G,O}}$ and $\hat{\mathcal{B}}_{\mathrm{G,T}}$ have similar distribution either in (a) or in (b).

When $\Delta_{min}^{\mathrm{SBP}}$ and $\Delta_{min}^{\mathrm{RR}}$ thresholds are imposed (regardeless the r_{min} value), there are 4/46 files without identified segments and, therefore, the BRS can not be estimated. Without $\Delta_{min}^{\mathrm{SBP}}$ and $\Delta_{min}^{\mathrm{RR}}$, these files present segments and the corresponding BRS analysis results are displayed with the circles in Figures 3(b). The N and K values decrease and r increases with increasing r_{min} values. These files present lower N and higher K comparing to the remaining files. The r values are higher than the remaining, probably due to the lower N and N/K. Finally, the corresponding $\hat{\mathcal{B}}$ are lower than the remaining, indicating a poorer BRS function for these cases.

Without enforcing $\Delta_{min}^{\mathrm{SBP}}$ and $\Delta_{min}^{\mathrm{RR}}$ thresholds, the value of r_{min}=0.8 (traditionally imposed for BSs identification) allows to achieve a trade-off between N and r, as N decreases and r increases for increasing r_{min}. As shown in Figures 3(b), r_{min}=0.8 makes available more than 50% of all beats presenting a correlation close to 0.8. The $\hat{\mathcal{B}}_{\mathrm{G,O}}$ and $\hat{\mathcal{B}}_{\mathrm{G,T}}$ values have similar distributions when obtained either imposing or not the $\Delta_{min}^{\mathrm{SBP}}$ and $\Delta_{min}^{\mathrm{RR}}$ thresholds. The apriori setting of r_{min}=0.8 leading to r close to 0.8 indicates stationarity of BRS over time in this dataset and supports the use of global/total approach for BRS estimation, which assume implicitly stationarity.

4. Conclusions

In this work, the effect of changing the thresholds values for the identification of baroreflex related segments in SBP and RR series is studied, with the goal of establish reference values. The results in the EuroBaVar dataset indicate that the simultaneous use of $\Delta^{\text{SBP}}_{min}$, Δ^{RR}_{min} and r_{min} can be avoided. BRS analysis from the traditional BSs ($\Delta^{\text{SBP}}_{min}$=1, Δ^{RR}_{min}=5 and r_{min}=0.8) presents 128 out of 512 beats, located typically in 3 beats length segments. Moreover, in 4/46 of the files it is not possible to identify BSs and the BRS can not be quantified.

Without imposing $\Delta^{\text{SBP}}_{min}$ and Δ^{RR}_{min} thresholds, the number of beats and identified segments is always higher, at the expense of a slight reduction in the global SBP–RR correlation. Also, BRS quantification is always possible, even for the files without BSs. With the unique setting of r_{min}=0.8 (traditionally imposed for BSs identification) the number of identified beats is higher than 256 out of 512 beats, located in longer segments. Also, there are no substantial changes in the BRS estimates distributions for global/total approach.

In short, time domain BRS estimation is improved by removing $\Delta^{\text{SBP}}_{min}$ and Δ^{RR}_{min} thresholds and setting r_{min}=0.8.

Acknowledgements

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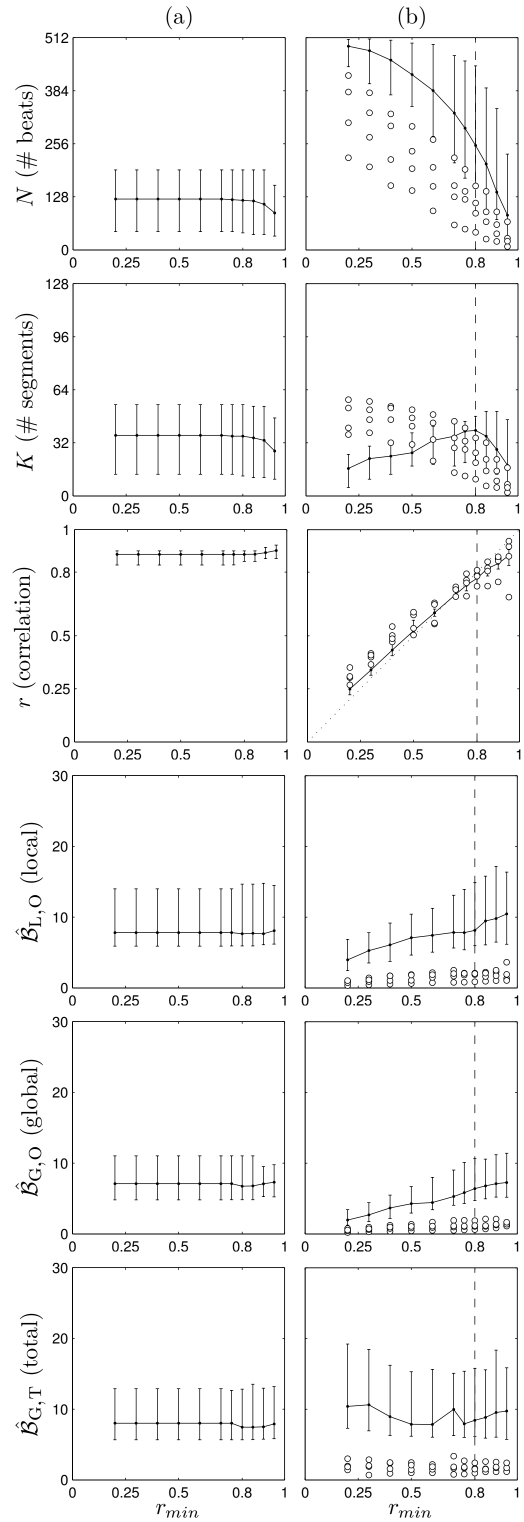

Figure 3. N, K, r and $\hat{\mathcal{B}}$ distribution as a function of r_{min} values, either (a) setting $\Delta^{\text{SBP}}_{min}$=1 and Δ^{RR}_{min}=5 or (b) removing $\Delta^{\text{SBP}}_{min}$ and Δ^{RR}_{min}. Bars represent quartiles and circles localize the files without identified segments for (a).