

Igor L. Popovych^{1,2,5}, Nataliya V. Kozyavkina¹, Liliya G. Barylyak^{2,5}, Yuliya V. Vovchyna³, Nataliya M. Voronych-Semchenko³, Walery Zukow⁴, Volodymyr V. Tsymbryla⁵. Variants of changes in blood pressure during its three consecutive registrations. *Journal of Education, Health and Sport*. 2022;12(4):365-375. eISSN 2391-8306. DOI <http://dx.doi.org/10.12775/JEHS.2022.12.04.032> <https://apcz.umk.pl/JEHS/article/view/39853> <https://zenodo.org/records/10552932>

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Variants of changes in blood pressure during its three consecutive registrations

Igor L. Popovych^{1,2,5}, Nataliya V. Kozyavkina¹, Liliya G. Barylyak^{2,5},
Yuliya V. Vovchyna³, Nataliya M. Voronych-Semchenko³, Walery Zukow⁴,
Volodymyr V. Tsymbryla⁵

¹Kozyavkin Rehabilitation Clinic, Truskavets', Ukraine clinic@kozyavkin.com

²OO Bohomolets' Institute of Physiology, Kyiv, Ukraine i.popovych@biph.kiev.ua;
liliabaryliak@gmail.com

³Ivano-Frankivs'k National Medical University, Ivano-Frankivs'k, Ukraine

⁴Nicolaus Copernicus University, Torun, Poland w.zukow@wp.pl

⁵Ukrainian Scientific Research Institute of Medicine of Transport, Odesa, Ukraine
cymbryla@gmail.com

Abstract

Introduction and aim. Earlier we noted that the patterns of blood pressure (BP) parameters recorded three times in a row deserve special attention. The aim of this article is to classify variants of changes in systolic and diastolic BP during its three consecutive registrations.

Material and methods. The object of observation were 20 volunteers: ten women and ten men aged 33-76 years with maladaptation. Systolic (Ps) and diastolic (Pd) BP was measured in a sitting position three times in a row without pause. Each patient was tested twice with a 7-day interval.

Results. We confirmed the diversity of Ps₂/Ps₁, Ps₃/Ps₁, Pd₂/Pd₁ and Pd₃/Pd₁ patterns identified earlier. 5 clusters were identified. The most characteristic feature of clusters are the changes in Pd during the second registration. Instead, the contribution of changes in Ps during the second registration is minimal. It was found that in 18 members of the most numerous cluster No1, Pd is practically stable, while Ps consistently falls with each subsequent measurement. In 8 members of cluster No.4, Pd

slightly but consistently decreases, and Ps slightly but consistently increases. In 4 members of cluster No.5, Pd significantly decreases at the second measurement and remains at this level at the third measurement; Ps reacts to measurements similarly, but less noticeably. In 7 members of cluster No.3, Pd significantly increases in the second measurement, but in the next one it only slightly exceeds the initial level, while Ps is practically stable. In 3 members of cluster No2, Pd increases even more during the second measurement and remains significantly higher than the initial one thereafter, while Ps steadily decreases.

Conclusion. In the process of successive three-time measurement of blood pressure, changes in its values, which differ in severity and direction, were found, grouped into 5 patterns. The following article will show that each pattern is characterized by a specific constellation of parameters of the neuroendocrine-immune complex and metabolism, which determines a certain reaction to the occlusion of the brachial arteries by the factors of vasoconstriction, vasodilatation and inotropism.

Keywords: Blood pressure, successive three-time measurement, five patterns.

Introduction

Earlier we [4,5] noted that the patterns of blood pressure (BP) parameters recorded three times in a row deserve special attention. We discovered that the level of Pd3/Pd1 ratio in patients with AH I is greater than 1.0 and the maximum for the sample. This is combined with an elevated level of general peripheral resistance of vessels (GPRV). In contrast, patients with Low Norm BP have a Pd3/Pd1 ratio less than 1.0 and are associated with low GPRV. Patients in the other three BP clusters (AH II, High Norm, and Norm) characterized by almost identical close to 1.0 Pd3/Pd1 ratio and normal GPRV levels.

Hence, it is suggested that in patients with AH I in response to triple occlusion of the shoulder arteries with a tonometer cuff, their endothelium increases the release of vasoconstrictors and/or reduces the release of vasodilators while in patients with Low Norm BP a similar procedure causes

increase the release of vasodilators and/or decrease the release of vasoconstrictors. It seems that vasodilation has a cholinergic nature and realizes by M₂-receptors [2]. In patients of other clusters, the balance of vasoconstrictors/vasodilators remains stable. Patients with AH I also had the highest level of Pd2/Pd1 ratio, while the lowest level was found in patients with Norm BP, combined with maximum levels of sympathetic markers. This suggests the realization of vasodilation through β_2 -adrenoceptors [2]. Maximal level of Ps3/Ps1 ratio in patients with High Norm BP indicates the minimum for the sample reduction of systolic BP in the third consecutive measurement, which we interpreted as the minimum release of vasodilators and/or maximum release of vasoconstrictors in response to occlusion.

The aim of this article is to classify variants of changes in systolic and diastolic BP during its three consecutive registrations.

Material and research methods

The object of observation were 20 volunteers: ten women and ten men aged 33-76 years without clinical diagnose but with dysfunction of neuro-endocrine-immune complex and metabolism, characteristic for maladaptation.

The main object of the study was BP. Systolic (Ps) and diastolic (Pd) BP was measured (by tonometer “Omron M4-I”, Netherlands) in a sitting position three times in a row without pause. Each patient was tested twice with a 7-day interval.

Results processed using the software package “Microsoft Excell” and "Statistica 6.4 Stat Soft Inc" (Tusla, OK, USA).

Results and discussion

On this sample, we confirmed the diversity of Ps2/Ps1, Ps3/Ps1, Pd2/Pd1 and Pd3/Pd1 patterns identified earlier. Therefore, the method of cluster analysis (k-mean clustering) [1] was used to create homogeneous groups.

5 clusters were identified, the members of which differ significantly from the members of other clusters (Table 1) and differ minimally from each other (Table 2, see Appendix).

Table 1. Euclidean Distances between Clusters

Cluster Number	Distances below diagonal Squared distances above diagonal				
	No. 1	No. 2	No. 3	No. 4	No. 5
No. 1	0,000	0,009	0,004	0,006	0,003
No. 2	0,096	0,000	0,005	0,017	0,022
No. 3	0,066	0,071	0,000	0,004	0,009
No. 4	0,075	0,129	0,061	0,000	0,004
No. 5	0,057	0,147	0,095	0,063	0,000

In the next stage carried Analysis of Variance and ranking variables for coefficient η^2 :

$$\eta^2 = S_b^2 / (S_b^2 + S_w^2); R = \eta; F = [S_b^2(n-k)] / [S_w^2(k-1)], \text{ where}$$

Sb^2 is Between Variance; Sw^2 is Within Variance; n is number of sample (40); k is number of groups-clusters (5).

It was found (Table 3) that the most characteristic feature of clusters are the changes in Pd during the second registration. The changes in Pd during the third registration make a slightly smaller contribution to the distribution of the sample into clusters. Instead, the contribution of changes in Ps during the second registration is minimal. Therefore, in the further analysis, the emphasis was placed on the dynamics of diastolic BP.

Table 3. Analysis of Variance

Variables	Between SS	Within SS	η^2	R	F	signif. p
Pd2/Pd1	0,1353	0.0328	0.805	0.897	36.1	10^{-6}
Pd3/Pd1	0,0677	0.0272	0.713	0.845	21.8	10^{-6}
Ps3/Ps1	0,0940	0.0548	0.632	0.795	15.0	10^{-6}
Ps2/Ps1	0,0464	0.0433	0.517	0.719	9.37	10^{-4}

It was found that in 18 members of the most numerous (45% of the sample) cluster No1, Pd is practically stable (Fig. 1), while Ps consistently falls with each subsequent measurement (Fig. 2), so we named this pattern D00S2-3-.

In 8 members of cluster No.4, Pd slightly but consistently decreases, and Ps slightly but consistently increases (pattern D01-S01+).

In 4 members of cluster No.5, Pd significantly decreases at the second measurement and remains at this level at the third measurement; Ps reacts to measurements similarly, but less noticeably (pattern D2-2-S1-1-).

In 7 members of cluster No.3, Pd significantly increases in the second measurement, but in the next one it only slightly exceeds the initial level, while Ps is practically stable (pattern D2+1+S00).

Finally, in 3 members of cluster No2, Pd increases even more during the second measurement and remains significantly higher than the initial one thereafter, while Ps steadily decreases (pattern D3+2+S2-2-).

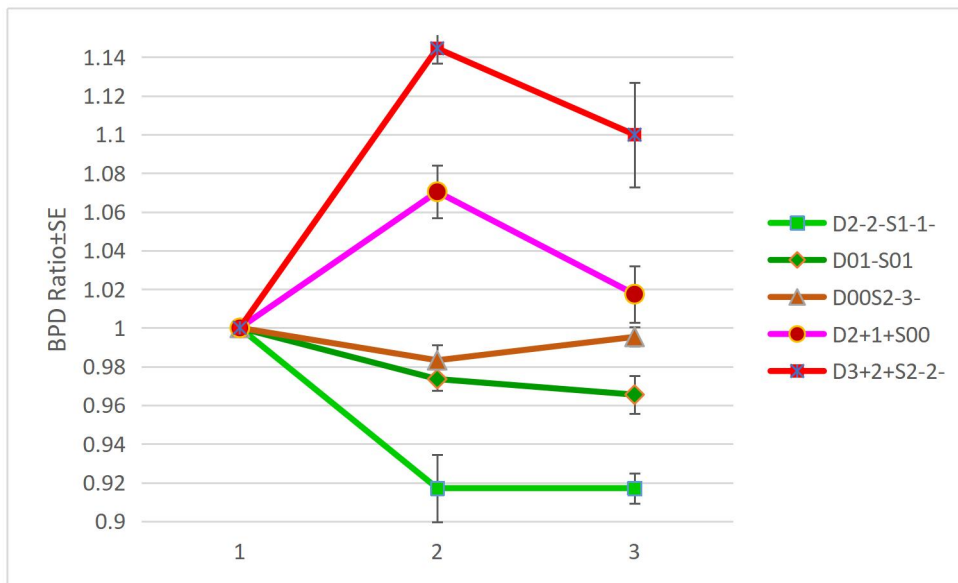


Fig. 1. The patterns of diastolic blood pressure

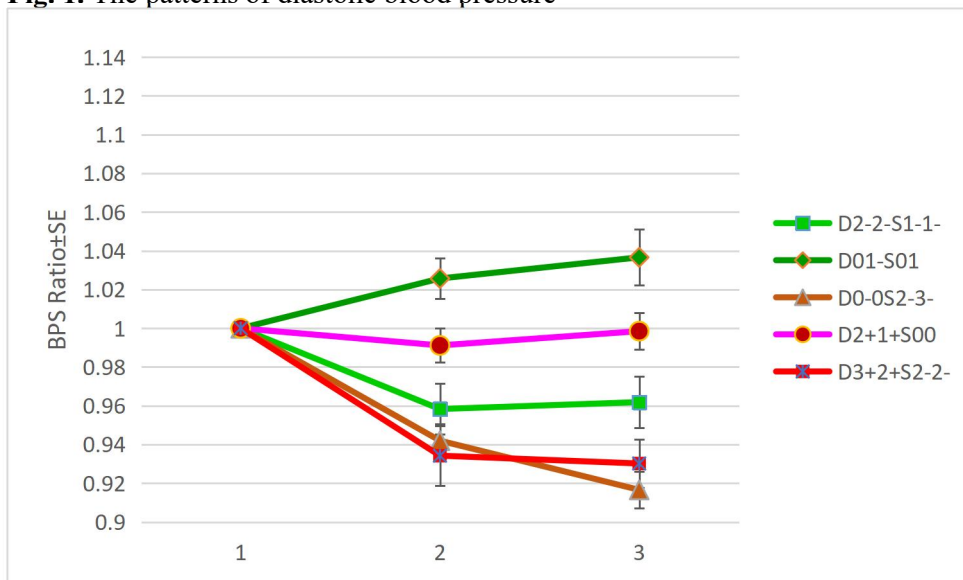


Fig. 2. The patterns of systolic blood pressure

In order to visualize clusters and each of their members, the information field of the mentioned parameters, as well as actual Pd and Ps values, was subjected to discriminant analysis using the forward stepwise method [3] (Tables 4 and 5).

Table 4. Discriminant Function Analysis Summary for Variables, their actual levels for Clusters as well as Reference levels and Coefficients of Variability

Step 6, N of vars in model: 6; Grouping: 5 grps; Wilks' Λ : 0.0229; approx. $F_{(24)}=8.6$; $p<10^{-6}$

Variables currently in the model	Blood Pressure Reaction Clusters (n)					Parameters of Wilk's Statistics					Reference (20)	Cv
	D 2-2-S 1-1- (4)	D 01-S 01+ (8)	D 1-0 S 2-3- (18)	D 2+1+ S 00 (7)	D 3+2+ S 2-2- (3)	Wilks Λ	Partial Λ	F-remove (4.30)	p-value	Tolerance		
BPd2/BPd1 ratio•1000	917 17	974 8	983 8	1070 14	1145 8	0,063	0,365	13,1	10^{-5}	0,914	0.986 0.016	0.071
BPs3/BPs1 ratio•1000	962 13	965 10	917 9	999 17	930 13	0,034	0,681	3,51	0,018	0,847	0.975 0.016	0.075
BPd3/BPd1 ratio•1000	917 8	1037 14	995 5	1017 15	1100 27	0,045	0,510	7,21	10^{-3}	0,898	0.971 0.009	0.041
BPs2/BPs1 ratio•1000	958 13	1026 10	942 9	991 16	934 15	0,028	0,809	1,77	0,161	0,874	0.985 0.011	0.051
BP Diastolic, mmHg	84.5 4.8	77.6 2.8	82.3 2.2	81.3 5.3	74.3 5.5	0,028	0,819	1,66	0,186	0,443	79.0 1.5	0.086
BP Systolic, mmHg	130 10	126 8	146 5	135 7	160 6	0,027	0,862	1,20	0,332	0,467	124.5 3.4	0.122

Note: Meam \pm SE are given for variables. Reference values are not subject to discriminant analysis.

Table 5. Summary of Stepwise Analysis for Variables, ranked by criterion Lambda

Variables currently in the model	F to enter	p-value	Λ	F-value	p-value
BPd2/BPd1 ratio	36,05	10^{-6}	0,195	36,05	10^{-6}
BPs3/BPs1 ratio	14,71	10^{-6}	0,072	23,28	10^{-6}
BPd3/BPd1 ratio	7,373	10^{-3}	0,038	17,88	10^{-6}
BPs2/BPs1 ratio	1,880	0,138	0,031	13,11	10^{-6}
BP Diastolic, mmHg	1,185	0,337	0,027	10,31	10^{-6}
BP Systolic, mmHg	1,198	0,332	0,023	8,617	10^{-6}

Next, the 6-dimensional space of discriminant variables transforms into 4-dimensional space of a canonical roots. The canonical correlation coefficient (r^*) as a measure of connection between clusters and discriminant function is for Root 1 0.947 (Wilks' $\Lambda=0.023$; $\chi^2_{(24)}=127$; $p<10^{-6}$), for Root 2 0.845 (Wilks' $\Lambda=0.223$; $\chi^2_{(192)}=167$; $p<10^{-5}$), for Root 3 0.430 (Wilks' $\Lambda=0.779$; $\chi^2_{(8)}=8.4$; $p=0.399$), and for Root 4 0.209 (Wilks' $\Lambda=0.956$; $\chi^2_{(3)}=1.5$; $p=0.681$). The first root contains 76.0% of discriminative opportunities, the second 21.6%, while the third 2.0%, and the last 0.4% only, therefore were ignored in the future.

The calculation of the discriminant root values for each person as the sum of the products of raw coefficients to the individual values of discriminant variables together with the constant (Table 6) enables the visualization of each patient in the information space of the roots (Fig. 3).

Table 6. Standardized and Raw Coefficients and Constants for Variables

Coefficients Variables currently in the model	Standardized		Raw	
	Root 1	Root 2	Root 1	Root 2
BPd2/BPd1 ratio	0.804	-0.312	26.25	-10.17
BPs3/BPs1 ratio	-0.120	-0.680	-3.032	-17.19
BPd3/BPd1 ratio	0.755	0.081	27.07	2.900
BPs2/BPs1 ratio	-0.258	-0.432	-7.331	-12.29
BP Diastolic, mmHg	-0.365	-0.027	-0.036	-0.003
BP Systolic, mmHg	0.121	0.335	0.006	0.017
	Constants		-41.12	33.62
	Eigenvalues		8.756	2.492
Cumulative proportions			0.760	0.976

Table 7 presents the full structural coefficients, that is, the coefficients of correlation between the discriminant root and variables. There are also average values (centroids) of roots and Z-scores of variables. Reference values for Z-scores calculated by BP ratios in persons with normal Ps and Pd levels (120÷129 mmHg and 77÷81 mmHg respectively). This enables correct comparison of variables expressed in different units and with different variability.

Table 7. Correlations Variables-Canonical Roots, Means of Roots and Z-scores of Variables

Variables currently in the model	Correlations Variables-Roots		D2-2- S1-1- (4)	D01- S01+ (8)	D1-0 S2-3- (18)	D2+1+ S00 (7)	D3+2+ S2-2- (3)
	R 1	R 2					
Root 1 (76.0%)	R 1	R 2	-4.41	-2.12	-0.12	2.12	7.33
BPd2/BPd1 ratio	0.657	-0.345	-0.99	0.17	0.36	2.14	3.66
BPd3/BPd1 ratio	0.528	0.040	-1.24	-0.27	0.32	0.76	2.40
BP Systolic, mmHg	0.122	0.241	0.36	0.09	1.42	0.67	2.32
BP Diastolic, mmHg	-0.048	0.101	0.84	-0.21	0.51	0.35	-0.71
Root 2 (21.6%)	R 1	R 2	0.58	-2.02	1.38	-1.64	0.15
BPs3/BPs1 ratio	-0.109	-0.803	0.04	0.94	-0.51	0.48	-0.35
BPs2/BPs1 ratio	-0.106	-0.614	-0.07	0.77	-0.27	0.34	-0.36

The localization along the first root axis in the extreme right (positive) zone (Fig. 2) of the members of cluster **D3+2+S2-2-** reflects maximum for sampling reactive increase of Pd; while the initial level of Pd is maximally reduced, and Ps is maximally increased.

At the opposite pole of the axis are the members of the **D2-2-S1-1-** cluster, which are characterized by the maximum reactive reduction of Pd, the initial level of which is the maximum for the sample.

The members of the rest of the clusters occupy intermediate positions along the axis and are not clearly demarcated from each other.

Instead, their separation occurs along the axis of the second root. The top position of cluster members **D1-0S2-3-** reflects the maximum for the sample Ps decrease in the process of triple registration, while Ps in members of clusters **D01-S01+** and **D2+1+S00** increases.

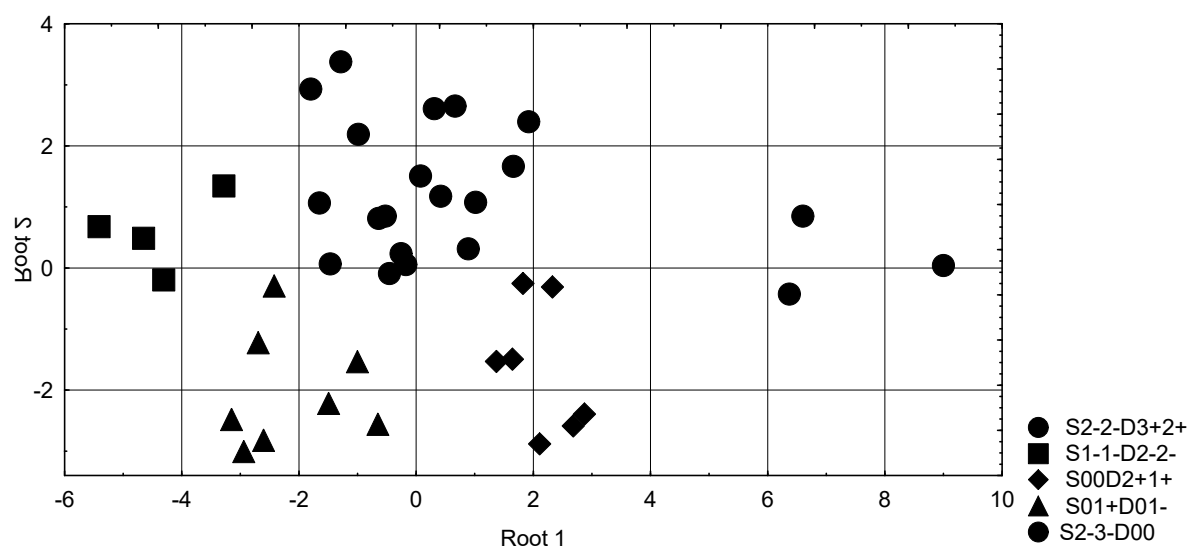


Fig. 3. Scattering of individual values of the first and second discriminant roots of patients of different BPR clusters

In general, all clusters are quite clearly delineated on the planes of two roots even, which is documented by calculating the Mahalanobis distances (Table 8).

Table 8. Squared Mahalanobis Distances between BPR Clusters, **F-values** (df=6.3) and p-levels

BPR Clusters	D3+2+ S2-2- (3)	D2-2- S1-1- (4)	D01- S01+ (8)	D2+1+ S00 (7)	D1-0 S2-3- (18)
D3+2+ S2-2-	0	139	94	32	57
D2-2- S1-1-	34 10 ⁻⁶	0	13	48	20
D01- S01+	29 10 ⁻⁶	5.1 10 ⁻³	0	20	16
D2+1+ S00	9.6 10 ⁻⁵	17 10 ⁻⁶	11 10 ⁻⁵	0	15
D1-0 S2-3-	21 10 ⁻⁶	9.2 10 ⁻⁵	12 10 ⁻⁶	11 10 ⁻⁵	0

The same discriminant parameters can be used to identify the belonging of one or another person to one or another cluster. This purpose of discriminant analysis is realized with the help of classifying functions (Table 9).

Table 9. Coefficients and Constants for Classification Functions for BPR Clusters

BP Clusters	Reactivity	D3+2+ S2-2-	D2-2- S1-1-	D2+1+ S00	D01- S01+	D00 S2-3-
Variables currently in the model		p=.075	p=.100	p=.175	p=.200	p=.450
BPd2/BPd1 ratio		1408	1112	1306	1179	1204
BPs3/BPs1 ratio		317,9	338,3	347,2	378,4	308,5
BPd3/BPd1 ratio		1582	1252	1429	1327	1386
BPs2/BPs1 ratio		409,8	487,8	478,5	514,9	459,5
BP Diastolic, mmHg		-0,43	0,11	-0,06	-0,06	-0,08
BP Systolic, mmHg		-0,20	-0,32	-0,34	-0,31	-0,26
Constants		-1985	-1467	-1813	-1655	-1618

Classification accuracy is 100% (Table 10).

Table 10. Classification matrix

Group	Rows: Observed classifications Columns: Predicted classifications					
	Percent Correct	S2-2-D3+2+ p=,075	S1-1-D2-2- p=,100	S00D2+1+ p=,175	S01D01- p=,200	S2-3-D00 p=,450
S2-2-D3+2+	100	3	0	0	0	0
S1-1-D2-2-	100	0	4	0	0	0
S00D2+1+	100	0	0	7	0	0
S01D01-	100	0	0	0	8	0
S2-3-D00	100	0	0	0	0	18
Total	100	3	4	7	8	18

Conclusion

So, in the process of successive three-time measurement of blood pressure, changes in its values, which differ in severity and direction, were found, grouped into 5 patterns. The following article will show that each pattern is characterized by a specific constellation of parameters of the neuroendocrine-immune complex and metabolism, which determines a certain reaction to the occlusion of the brachial arteries by the factors of vasoconstriction, vasodilatation and inotropism.

Acknowledgment

We express sincere gratitude to colleagues of sanatoria “Kryshtalevyi Palats” and “Moldova” for help in conducting this investigation.

Accordance to ethics standards

Tests in patients are conducted in accordance with positions of Helsinki Declaration 1975, revised and complemented in 2002, and directive of National Committee on ethics of scientific researches. During realization of tests from all parent of participants the informed consent is got and used all measures for providing of anonymity of participants. For all authors any conflict of interests is absent.

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Appendix

Table 2. Members of Clusters and Distances from Respective Cluster Center

Members of Cluster Number 1 (D00S2-3-) and Distances from Respective Cluster Center Cluster contains 18 cases	
Case No.	Distance
C 2	0,026
C 5	0,049
C 6	0,032
C 8	0,046
C 9	0,029
C 11	0,041
C 13	0,043
C 14	0,015
C 18	0,021
C 19	0,050
C 22	0,036
C 23	0,033
C 32	0,016
C 33	0,019
C 34	0,027
C 35	0,017
C 37	0,032
C 40	0,022

Members of Cluster Number 5 (D2-2-S1-1-) and Distances from Respective Cluster Center Cluster contains 4 cases	
Case No.	Distance
C 20	0,021
C 24	0,017
C 27	0,025
C 36	0,028

Members of Cluster Number 4 (D1-1-S01+) and Distances from Respective Cluster Center Cluster contains 8 cases	
Case No.	Distance
C 3	0,043
C 10	0,023
C 15	0,027
C 21	0,021
C 25	0,022
C 29	0,034
C 30	0,022
C 31	0,026

Members of Cluster Number 2 (D3+2+S2-2-) and Distances from Respective Cluster Center Cluster contains 3 cases	
Case No.	Distance
C 17	0,026
C 38	0,026
C 39	0,021

	Members of Cluster Number 3 (D2+1+S00) and Distances from Respective Cluster Center Cluster contains 7 cases	
Case No.	Distance	
C 1	0,033	
C 4	0,031	
C 7	0,022	
C 12	0,049	
C 16	0,012	
C 26	0,051	
C 28	0,048	