ORIGINAL ARTICLE

Leukocyte Cell Population Data (CPD) as a Discriminating Tool between Active Tuberculosis and Lung Cancer

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SUMMARY

Background: Cell population data (CPD) are parameters of cell size, shape, and content that can be used in the differential diagnosis of diseases such as leukemia, bacterial or viral infection, and dengue fever. The aim of this study was to screen for CPD parameters that can be used to differentiate active pulmonary tuberculosis (APTB) from lung cancer (LC) and to assess their efficacy.
Methods: Whole blood samples from 84 APTB patients, 109 LC patients, and 95 healthy volunteers were collected from January 2019 to November 2019. All samples were tested by DxH800 blood cell analyzer using VCS (volume, conductivity, and scatter) technology to obtain CPD parameters, total leukocyte count, and leukocyte classification count. The results were tested for normal distribution, followed by one-way analysis of variance (ANOVA) and area under the ROC curve (AUC) analysis to evaluate the diagnostic efficacy of CPD parameters.
Results: Twenty-three CPD parameters were significantly higher in the APTB group than in the LC group, 13 CPD parameters were significantly lower than in the LC group, and 6 CPD parameters were not statistically different between the two groups. The AUCs of CPD parameters between the APTB and LC groups were analyzed, and the results showed that the AUCs of nine CPD parameters were higher than 0.91, with the AUCs of neutrophil mean conductance (NMC), lymphocyte mean conductance (LMC), and monocyte mean conductance (MMC) even reaching 0.983, 0.930, and 0.996, respectively. Meanwhile, compared with the CPD parameters, white blood cells and their conventional differential counts (WBC, NE%, LY%, MO%) did not result in higher AUCs for the two groups (0.641, 0.757, 0.659, 0.733, respectively).
Conclusions: Three CPD parameters (NMC, LMC, and MMC) obtained higher AUC than other indicators, and their combined diagnosis efficacy obtained 100% sensitivity and 99.1% specificity, which may be helpful for clinical differential diagnosis of APTB and LC.
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Supplementary Data

Table S1. **Demographic details and hematological parameters in APTB, LC, and HC groups.**

Indicator	APTB (n = 84)	LC (n = 109)	HC (n = 95)	APTB vs. LC	APTB vs. HC	LC vs. HC
WBC (10^9/L)	6.656 ± 2.383	9.255 ± 7.198	7.169 ± 2.796	0.0021	NS	0.0169
NE%	64.18 ± 9.191	74.33 ± 11.01	68.72 ± 12.57	< 0.0001	0.0046	0.0007
LY%	20.70 ± 8.047	15.98 ± 8.577	21.41 ± 10.38	0.0004	NS	< 0.0001
MO%	9.896 ± 3.521	7.234 ± 2.721	7.378 ± 2.556	< 0.0001	< 0.0001	NS
Neutrophil CPD parameters						
NMV	144.2 ± 6.331	152.8 ± 11.22	156.6 ± 5.309	< 0.0001	< 0.0001	0.0013
NMV-SD	20.77 ± 3.166	34.05 ± 20.82	17.08 ± 1.126	< 0.0001	NS	< 0.0001
NMC	153.7 ± 2.726	143.2 ± 4.391	139.3 ± 1.783	< 0.0001	< 0.0001	< 0.0001
NMC-SD	9.587 ± 3.969	4.914 ± 1.191	4.395 ± 0.605	< 0.0001	< 0.0001	NS
N-MALS	133.7 ± 5.495	141.4 ± 5.890	145.3 ± 2.969	< 0.0001	< 0.0001	< 0.0001
N-MALS-SD	15.55 ± 5.231	10.56 ± 1.695	9.035 ± 0.733	< 0.0001	< 0.0001	0.0004
N-UMALS	137.7 ± 4.582	134.8 ± 5.416	139.2 ± 3.942	< 0.0001	0.0291	< 0.0001
N-UMALS-SD	14.99 ± 4.514	11.60 ± 1.475	9.849 ± 0.727	< 0.0001	< 0.0001	< 0.0001
N-LMALS	125.7 ± 8.658	139.1 ± 8.434	143.4 ± 3.147	< 0.0001	< 0.0001	< 0.0001
N-LMALS-SD	19.49 ± 5.229	12.84 ± 2.602	10.73 ± 0.884	< 0.0001	< 0.0001	< 0.0001
N-LALS	152.8 ± 19.11	152.8 ± 11.22	141.7 ± 5.451	NS	< 0.0001	< 0.0001
N-LALS-SD	42.16 ± 6.139	29.11 ± 5.854	23.95 ± 1.281	< 0.0001	< 0.0001	< 0.0001
N-AL2	143.0 ± 4.013	141.9 ± 11.50	140.6 ± 5.557	NS	NS	NS
N-AL2-SD	16.40 ± 4.247	9.723 ± 2.073	8.903 ± 1.171	< 0.0001	< 0.0001	0.0317
Lymphocyte CPD parameters						
LMV	89.32 ± 4.605	90.71 ± 5.280	93.63 ± 3.641	0.0388	< 0.0001	< 0.0001
LMV-SD	17.78 ± 3.895	14.92 ± 2.116	14.24 ± 1.194	< 0.0001	< 0.0001	NS
LMC	119.9 ± 3.264	113.4 ± 3.178	109.8 ± 1.785	< 0.0001	< 0.0001	< 0.0001
LMC-SD	13.27 ± 2.392	7.870 ± 2.372	6.882 ± 1.079	< 0.0001	< 0.0001	0.0007
L-MALS	60.86 ± 6.540	61.53 ± 7.437	69.66 ± 2.525	NS	< 0.0001	< 0.0001
L-MALS-SD	19.75 ± 2.717	17.46 ± 2.089	14.81 ± 0.663	< 0.0001	< 0.0001	< 0.0001
L-UMALS	63.48 ± 8.276	53.97 ± 11.84	63.93 ± 4.293	< 0.0001	NS	< 0.0001
L-UMALS-SD	21.96 ± 2.077	21.30 ± 2.263	17.51 ± 1.029	0.0164	< 0.0001	< 0.0001
L-LMALS	53.83 ± 6.014	57.46 ± 5.685	65.13 ± 2.038	< 0.0001	< 0.0001	< 0.0001
L-LMALS-SD	21.48 ± 1.733	20.25 ± 1.602	17.71 ± 0.656	< 0.0001	< 0.0001	< 0.0001
L-LALS	39.70 ± 3.173	35.72 ± 2.505	35.02 ± 1.313	< 0.0001	< 0.0001	0.0395
L-LALS-SD	14.87 ± 2.535	10.42 ± 2.330	8.637 ± 0.551	< 0.0001	< 0.0001	< 0.0001
L-AL2	75.55 ± 2.877	77.33 ± 2.715	76.57 ± 1.982	< 0.0001	0.0158	0.0341
L-AL2-SD	12.77 ± 2.692	10.93 ± 0.994	10.41 ± 0.527	< 0.0001	< 0.0001	0.0212

Table S1. Demographic details and hematological parameters in APTB, LC, and HC groups (continued).

Indicator	APTB (n = 84)	LC (n = 109)	HC (n = 95)	APTB vs. LC	APTB vs. HC	LC vs. HC
Monocyte CPD parameters						
MMV	183.0 ± 11.73	173.8 ± 12.41	176.0 ± 4.967	< 0.0001	< 0.0001	NS
MMV-SD	22.10 ± 2.519	20.25 ± 3.654	17.67 ± 1.458	< 0.0001	< 0.0001	< 0.0001
MMC	132.8 ± 2.309	122.4 ± 3.056	118.7 ± 1.764	< 0.0001	< 0.0001	< 0.0001
MMC-SD	7.380 ± 3.252	5.668 ± 1.336	4.875 ± 1.041	< 0.0001	< 0.0001	0.0057
M-MALS	83.90 ± 3.328	83.39 ± 6.498	90.97 ± 2.210	NS	< 0.0001	< 0.0001
M-MALS-SD	10.91 ± 1.429	12.86 ± 1.981	11.07 ± 1.036	< 0.0001	NS	< 0.0001
M-UMALS	94.04 ± 5.500	87.70 ± 9.109	93.51 ± 2.767	< 0.0001	NS	< 0.0001
M-UMALS-SD	11.83 ± 2.026	13.52 ± 2.108	11.81 ± 1.122	< 0.0001	NS	< 0.0001
M-LMALS	70.79 ± 2.816	74.05 ± 6.199	83.65 ± 2.551	< 0.0001	< 0.0001	< 0.0001
M-LMALS-SD	13.78 ± 1.232	16.82 ± 2.721	13.58 ± 1.062	< 0.0001	NS	< 0.0001
M-LALS	80.85 ± 11.08	78.18 ± 11.87	79.60 ± 5.667	NS	NS	NS
M-LALS-SD	22.50 ± 2.330	26.11 ± 5.006	18.58 ± 2.163	< 0.0001	< 0.0001	< 0.0001
M-AL2	131.5 ± 5.205	135.9 ± 5.492	133.9 ± 3.122	< 0.0001	0.0014	0.0036
M-AL2-SD	12.37 ± 2.340	12.98 ± 2.210	12.01 ± 1.729	NS	NS	0.0034

NS - no significance, APTB - active pulmonary tuberculosis, LC - lung cancer, HC - healthy control, WBC - white blood cell, NE% - neutrophil percentage, LY% - lymphocyte percentage, MO% - monocyte percentage, CPD - cell population data, NMV - neutrophil mean volume, NMV-SD - neutrophil mean volume standard deviation, NMC - neutrophil mean conductivity, NMC-SD - neutrophil mean conductivity standard deviation, N-MALS - neutrophil medium angle light scatter, N-MALS-SD - neutrophil medium angle light scatter standard deviation, N-UMALS - neutrophil upper medium angle light scatter, N-UMALS-SD - neutrophil upper medium angle light scatter standard deviation, N-LMALS - neutrophil lower medium angle light scatter, N-LMALS-SD - neutrophil lower medium angle light scatter standard deviation, N-LALS - neutrophil lower angle light scatter, N-LALS-SD - neutrophil lower angle light scatter standard deviation, N-AL2 - neutrophil axial light loss, N-AL2-SD - neutrophil axial light loss standard deviation, LMV - lymphocyte mean volume, LMV-SD - lymphocyte mean volume standard deviation, LMC - lymphocyte mean conductivity, LMC-SD - lymphocyte mean conductivity standard deviation, L-UMALS - lymphocyte upper median angle light scatter, L-UMALS-SD - lymphocyte upper median angle light scatter standard deviation, L-MALS - lymphocyte medium angle light scatter, L-MALS-SD - lymphocyte medium angle light scatter standard deviation, L-LMALS - lymphocyte lower median angle light scatter, L-LMALS-SD - lymphocyte lower median angle light scatter standard deviation, L-LALS - lymphocyte lower angle light scatter, L-LALS-SD - lymphocyte lower angle light scatter standard deviation, L-AL2 - lymphocyte axial light loss, L-AL2-SD - lymphocyte axial light loss standard deviation, MMV - monocyte mean volume, MMV-SD - monocyte mean volume standard deviation, MMC - monocyte mean conductivity, MMC-SD - monocyte mean conductivity standard deviation, M-UMALS - monocyte upper median angle light scatter, M-UMALS-SD - monocyte upper median angle light scatter standard deviation, M-MALS - monocyte medium angle light scatter, M-MALS-SD - monocyte medium angle light scatter standard deviation, M-LMALS - monocyte lower median angle light scatter, M-LMALS-SD - monocyte lower median angle light scatter standard deviation, M-LALS - monocyte lower angle light scatter, M-LALS-SD - monocyte lower angle light scatter standard deviation, M-AL2 - monocyte axial light loss, M-AL2-SD - monocyte axial light loss standard deviation.

Table S2. Diagnostic accuracy of the single conventional hematological indicator and the single CPD parameter (APTB vs. LC).

Parameter	AUC (95% CI)	Cutoff value	Sensitivity (%)	Specificity (%)
WBC	0.618 (0.539 - 0.697)	> 8.456	44.44	83.33
NE%	0.757 (0.691 - 0.823)	> 72.80	60.19	83.51
LY%	0.659 (0.585 - 0.733)	< 14.25	48.15	82.47
MO%	0.739 (0.667 - 0.810)	< 8.950	75.23	63.1
NMC	0.983 (0.967 - 0.998)	< 149.5	96.33	94.05
NMC-SD	0.938 (0.907 - 0.968)	< 5.645	82.57	92.86
N-LMALS-SD	0.916 (0.876 - 0.956)	< 14.37	86.24	88.1

Table S2. Diagnostic accuracy of the single conventional hematological indicator and the single CPD parameter (APTB vs. LC) (continued).

Parameter	AUC (95% CI)	Cutoff value	Sensitivity (%)	Specificity (%)
N-LALS-SD	0.936 (0.900 - 0.972)	< 30.94	82.57	98.81
N-AL2-SD	0.951 (0.921 - 0.981)	< 11.14	87.16	95.24
LMC	0.930 (0.895 - 0.965)	< 115.5	78.9	94.05
LMC-SD	0.946 (0.912 - 0.980)	< 9.895	88.99	95.24
L-LALS-SD	0.958 (0.929 - 0.987)	< 12.04	91.74	96.43
MMC	0.996 (0.989 - 1.000)	< 128.5	98.17	97.62
NMV	0.755 (0.689 - 0.821)	> 146.5	73.39	67.03
NMV-SD	0.528 (0.444 - 0.613)	> 34.24	40.37	100
N-MALS	0.848 (0.792 - 0.903)	> 139.5	72.48	85.71
N-MALS-SD	0.892 (0.846 - 0.938)	< 11.59	86.24	84.52
N-UMALS	0.654 (0.578 - 0.731)	< 137.5	69.72	55.95
N-UMALS-SD	0.771 (0.705 - 0.838)	< 12.61	80.73	61.9
N-LMALS	0.896 (0.851 - 0.942)	> 136.5	74.31	92.86
N-LALS	0.538 (0.449 - 0.628)	< 157.5	77.06	45.24
N-AL2	0.525 (0.442 - 0.608)	< 143.5	57.8	53.57
LMV	0.574 (0.494 - 0.655)	> 92.50	36.7	80.95
LMV-SD	0.764 (0.694 - 0.834)	< 16.37	86.24	61.9
L-MALS	0.536 (0.455 - 0.618)	> 64.50	37.61	76.19
L-MALS-SD	0.787 (0.723 - 0.851)	< 18.44	75.23	67.86
L-UMALS	0.728 (0.658 - 0.797)	< 56.50	55.05	84.52
L-UMALS-SD	0.568 (0.487 - 0.649)	< 19.17	21.1	94.05
L-LMALS	0.669 (0.592 - 0.746)	> 54.50	66.97	58.33
L-LMALS-SD	0.698 (0.624 - 0.772)	< 20.15	52.29	77.38
L-LALS	0.836 (0.776 - 0.895)	< 41.50	100	100
L-AL2	0.665 (0.589 - 0.742)	> 76.50	61.47	61.9
L-AL2-SD	0.787 (0.718 - 0.857)	< 11.36	78.9	73.81
MMV	0.703 (0.631 - 0.777)	< 168.5	39.45	95.24
MMV-SD	0.684 (0.609 - 0.760)	< 21.05	66.97	70.24
MMC-SD	0.799 (0.736 - 0.861)	< 5.615	64.22	89.29
M-MALS	0.519 (0.436 - 0.601)	< 79.50	27.52	95.24
M-MALS-SD	0.799 (0.736 - 0.862)	> 11.88	66.97	83.33
M-UMALS	0.723 (0.651 - 0.795)	< 88.50	51.38	96.43
M-UMALS-SD	0.755 (0.685 - 0.824)	> 12.15	71.56	72.62
M-LMALS	0.699 (0.624 - 0.774)	> 72.50	64.22	80.95
M-LMALS-SD	0.848 (0.793 - 0.903)	> 15.49	71.56	91.67
M-LALS	0.528 (0.446 - 0.609)	< 73.50	32.11	79.76
M-LALS-SD	0.718 (0.646 - 0.790)	> 26.09	49.54	91.67
M-AL2	0.734 (0.663 - 0.806)	> 133.5	67.89	72.62
M-AL2-SD	0.617 (0.537 - 0.697)	> 11.84	70.64	57.14