

## Anti-inflammatory Effects and Decreased Formation of Neutrophil Extracellular Traps by Enoxaparin in COVID-19 Patients

Supplemental Table S1:

Plasma levels of NET products and IL-8 in COVID-19 patients and NET formation induced by COVID-19 plasma.

Figure	Parameter	Healthy control	Mild case	Moderate case	Severe case	<i>p</i> -value vs Healthy control
1A	dsDNA	17.84 (15-21)	23.38 (19-26)	22.73 (14-31)	36.32 (27-39)	< 0.05 at Severe
1B	NE	88.49 (59-117)	105.91 (57-158)	150.50 (140-163)	169.08 (161-175)	< 0.05 at Severe and Moderate
1C	Histone-DNA complexes	0.039 (0.037-0.043)	0.033 (0.027-0.044)	0.398 (0.262-0.612)	1.145 (1.049-1.264)	< 0.05 at Severe and Moderate
1D	MPO-DNA complexes	0.023 (0.020-0.027)	0.059 (0.023-0.148)	0.128 (0.222-0.119)	0.243 (0.183-0.285)	< 0.05 at Severe
1E	IL-8	6.50 (5.20-7.31)	8.41 (5.65-14.78)	11.14 (6.74-18.26)	18.12 (10.00-25.22)	< 0.05 at Severe
1G	%NETs counting	38.58 (32-48)	62.25 (50-74)	73.25 (61-86)	80.75 (74-88)	< 0.05 at Severe and Moderate
1H	dsDNA	90.54 (74.06-105.01)	110.66 (98.63-135.93)	120.82 (106.46-130.05)	121.84 (114.64-127.14)	< 0.05 at Severe and Moderate

Supplemental Table S2:

The effect of enoxaparin pretreatment on NETs induced by COVID-19 plasma in vitro.

Figure	Parameter	Plasma alone	ENOX 0.5 IU/ml	ENOX 1.0 IU/ml	ENOX 2.0 IU/ml	<i>p</i> -value vs Plasma alone
2B	%NETs counting	54.1 (48.3-61.0)	33.9 (32.1-36.2)	26.7 (21.8-32.7)	27.5 (25.4-30.6)	<0.05 at ENOX 1.0 and 2.0 IU/ml
2C	dsDNA	124.37 (100.41-150.00)	123.44 (97.13-155.92)	109.14 (86.60-139.81)	105.06 (85.13-126.74)	<0.05 at ENOX 1.0 and 2.0 IU/ml
2D	NE	120.86 (117.94-126.95)	121.06 (117.83-125.54)	119.95 (116.87-124.02)	117.56 (112.21-120.82)	<0.05 at ENOX 2.0 IU/ml
2E	Histone-DNA complexes	0.21 (0.11-0.32)	0.11 (0.04-0.30)	0.14 (0.07-0.19)	0.06 (0.05-0.03)	<0.05 at ENOX 2.0 IU/ml
Figure	Parameter	Untreated	Healthy plasma	COVID-19 plasma	COVID-19 plasma+ENOX 2.0 IU/ml	<i>p</i> -value COVID-19 plasma vs COVID-19 plasma+ENOX 2.0 IU/ml
2F	<i>PAD4</i> gene expression	1.00	1.03 (0.60-1.51)	1.65 (1.57-1.79)	1.20 (0.95-1.23)	<i>Ns</i>
2G	<i>RELA</i> gene expression	1.00	1.33	2.73	1.44	<0.05

			(1.11-1.78)	(1.55-3.62)	(1.23-1.54)	
2H	SYK gene expression	1.00	1.64	2.10	1.02	<0.05
			(1.03-2.76)	(1.39-2.50)	(0.65-1.53)	
2I	PKC gene expression	1.00	1.54	1.65	1.03	<0.05
			(1.88-1.94)	(1.21-1.95)	(0.82-1.23)	
2J	ERK gene expression	1.00	1.60	2.31	0.97	<0.05
			(1.10-2.23)	(1.62-2.71)	(0.81-1.10)	

**Supplemental Table S3:**

**The effect of enoxaparin prophylaxis in COVID-19 patients on NETs and expression of inflammatory markers in COVID-19 patients.**

Figure	Parameter	Before Enoxaparin	After Enoxaparin	p-value
3A	TNF- $\alpha$	96.17	43.97	Ns
		(22.68-183.796)	(21.20-61.52)	
3B	IL-8	21.36	12.93	<0.05
		(17.17-23.04)	(6.30-17.39)	
3C	IL-6	29.20	3.00	<0.05
		(19.5-42.5)	(1.99-4.98)	
3D	Procalcitonin	0.69	0.15	<0.05
		(0.31-1.32)	(0.04-0.42)	
3E	hs-CRP	97.32	47.24	Ns
		(8.56-154.85)	(4.43-96.84)	
3F	Neutrophil (%)	85.13	85.08	Ns
		(79.6-90.3)	(83.3-85.7)	
3H	%NET	10.5	9.5	Ns
		(7.0-14.0)	(5.0-13.0)	
3I	dsDNA	698.53	659.63	Ns
		(553.46-1001.35)	(536.44-735.72)	
3J	NE	156.76	163.97	Ns
		(137.30-170.96)	(156.67-172.17)	
3K	MPO-DNA complexes	0.19	0.17	Ns
		(0.05-0.29)	(0.07-0.19)	
3L	PAD4 gene expression	1.00	0.52	Ns
			(0.19-0.87)	
3M	RELA gene expression	1.00	0.604	<0.05
			(0.39-0.80)	
3N	SYK gene expression	1.00	0.58	<0.05
			(0.50-0.67)	
3O	PKC gene expression	1.00	0.70	Ns
			(0.38-1.02)	

3P	ERK gene expression	1.00	0.70	<0.05
(0.50-0.87)				

**Supplemental Table S4:**

**Living guidance for clinical management of COVID-19<sup>1</sup> by the World Health Organization (WHO)**

Group	Definition	Details
Mild	No pneumonia	<ul style="list-style-type: none"> <li>- asymptomatic group or symptomatic without evidence of viral pneumonia or hypoxia</li> <li>- most experience of mild symptoms are fever, cough, fatigue, anorexia, shortness of breath, myalgias. Other non-specific symptoms, such as sore throat, nasal congestion, headache, diarrhea, nausea, and vomiting</li> </ul>
Moderate	Moderate Pneumonia	- clinical signs of pneumonia (fever, cough, dyspnea, fast breathing) but not severe including with SpO <sub>2</sub> ≥ 90% on room air
Severe	Severe pneumonia or ARDS	<ul style="list-style-type: none"> <li>- clinical signs of severe pneumonia (cough or difficulty in breathing + fast breathing or chest wall indrawing) including SpO<sub>2</sub> &lt; 90% on room air</li> <li>- chest imaging: (radiograph, CT scan, or lung ultrasound): bilateral opacities, not fully explained by volume overload, lobar or lung collapse, or nodules</li> </ul>