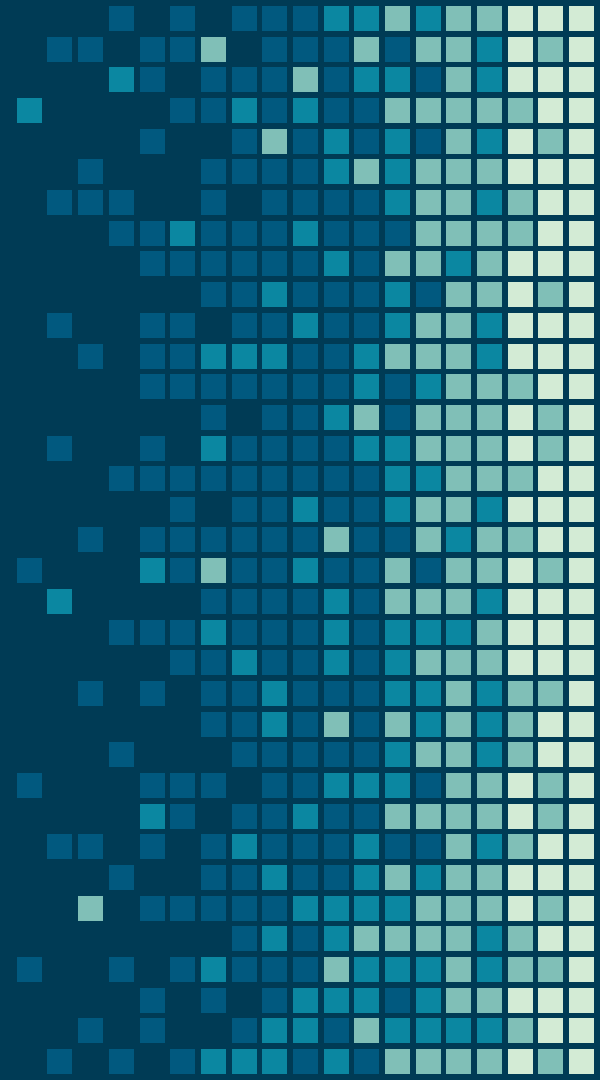


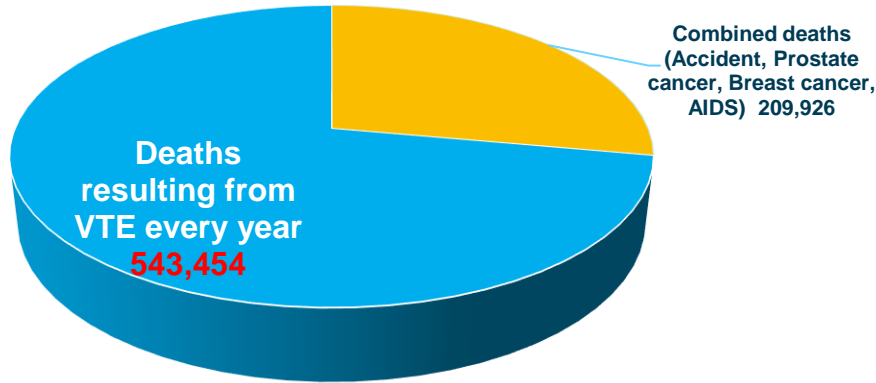
Cellular Indices of DVT

Anvit Divekar and Abhinav Paknikar
Mentor: Neha Thomas
GTF Group

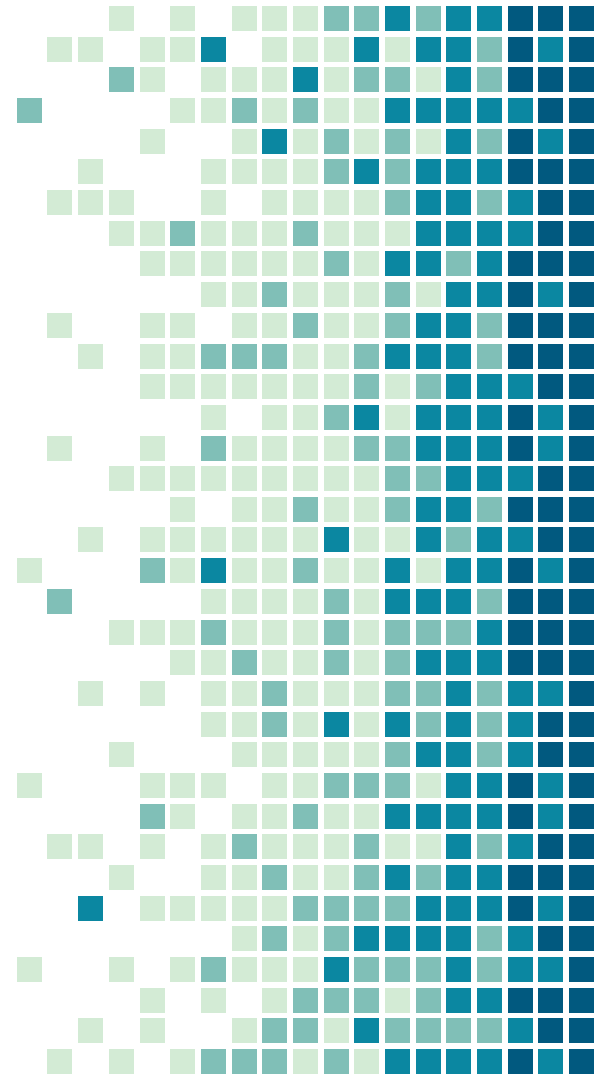


DEEP VEIN THROMBOSIS (DVT)

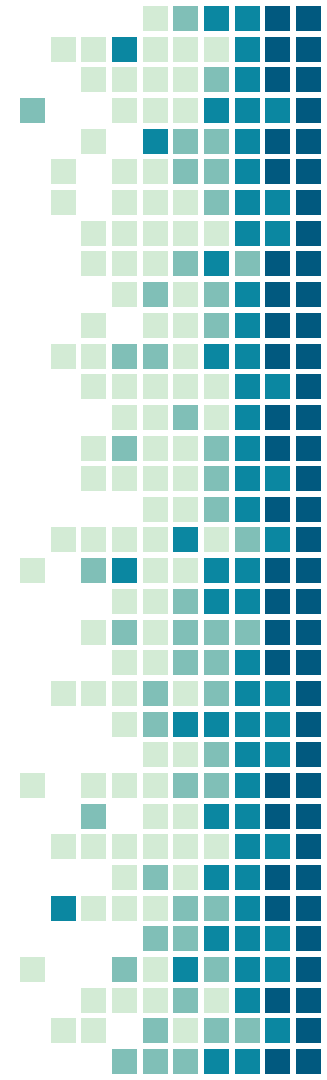
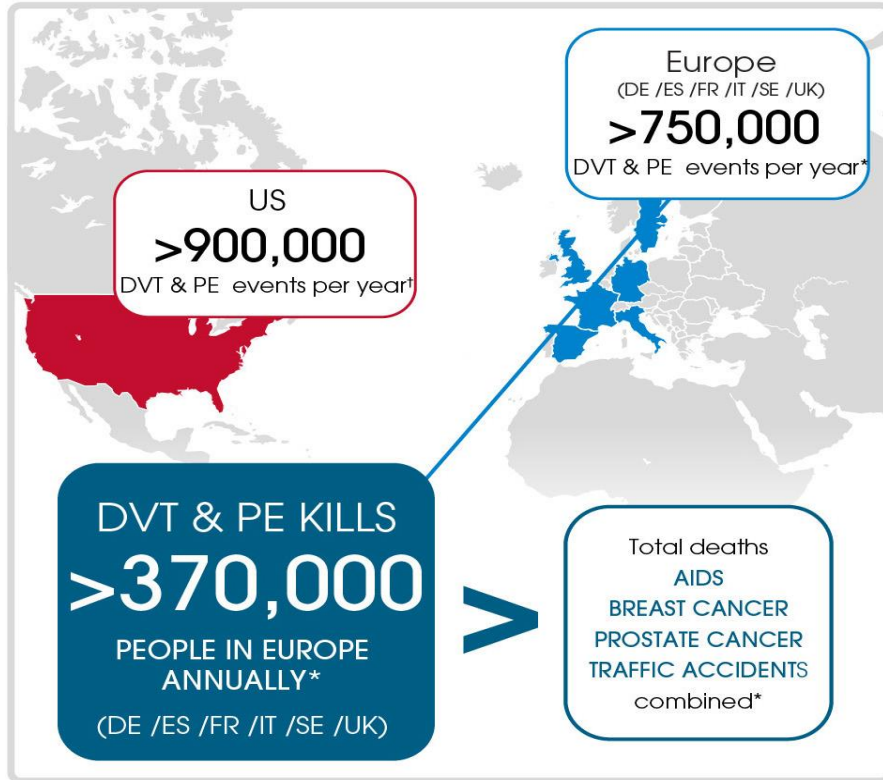
- DVT is one of the most common and serious forms of Venous Thromboembolism (VTE).
- DVT can cause serious complications if the clots travel to the lungs resulting in Pulmonary Embolism (PE).
- DVT + PE = VTE



Data obtained from ISTH Steering Committee for World Thrombosis Day, 2014.

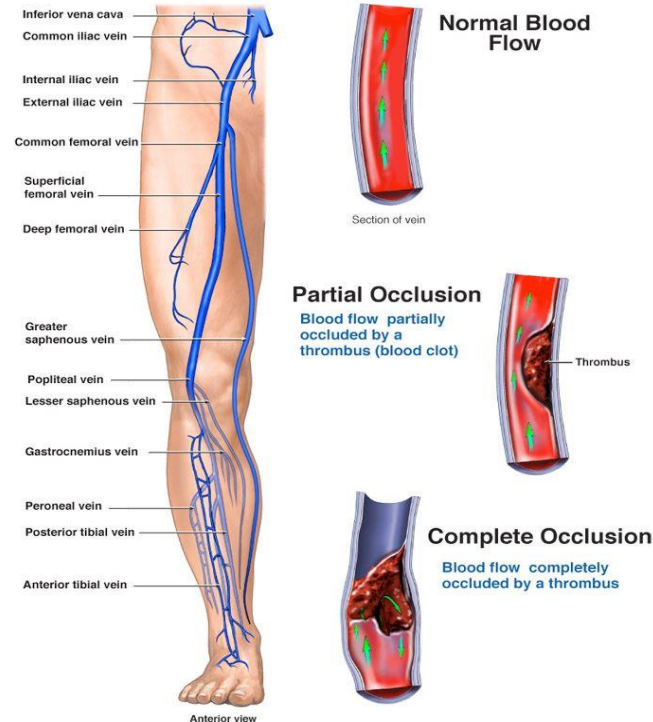


DVT and PE incidence rates worldwide



DEEP VEIN THROMBOSIS (DVT)

- DVT is a condition where clotting of blood takes place in a deep vein of an extremity, usually a vein in the leg (calf or thigh).
- A blood clot develops in these deep veins.

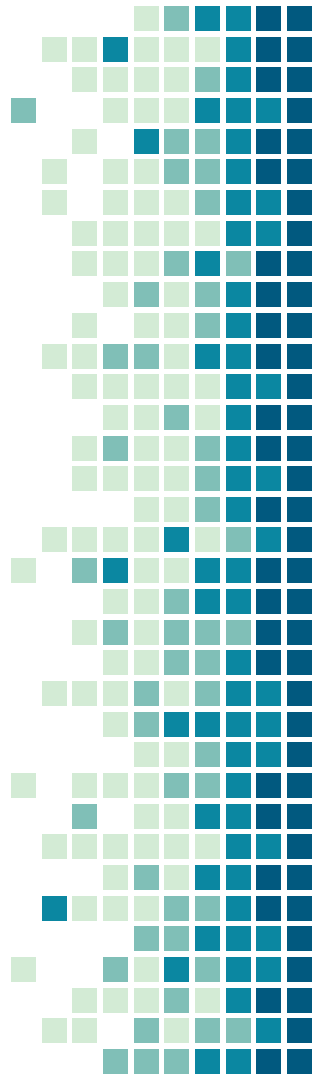
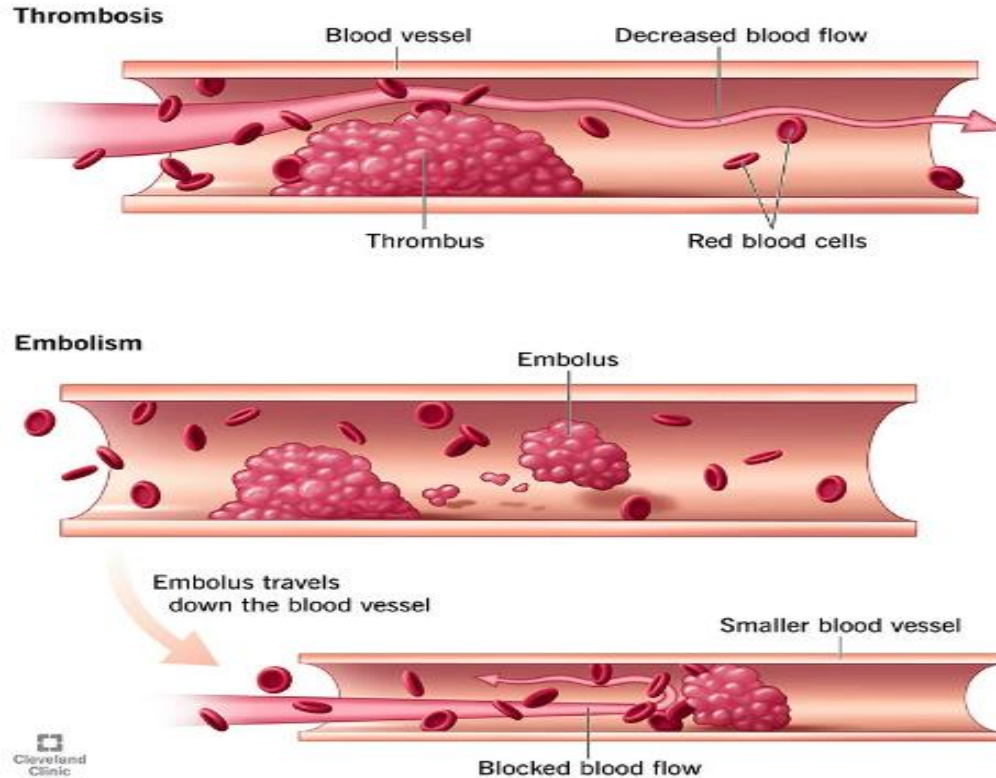


DVT

- DVT may occur suddenly (acute) or develop gradually (chronic).
- Serious medical condition, as if the thrombus breaks free it can travel to the lungs and heart which will eventually lead to a heart attack, stroke or pulmonary embolism (PE).
- Requires urgent medical treatment as soon as DVT is suspected and diagnosed.



PATHOPHYSIOLOGY OF DVT





immobility



birth control use



pregnancy/
postpartum



genetics



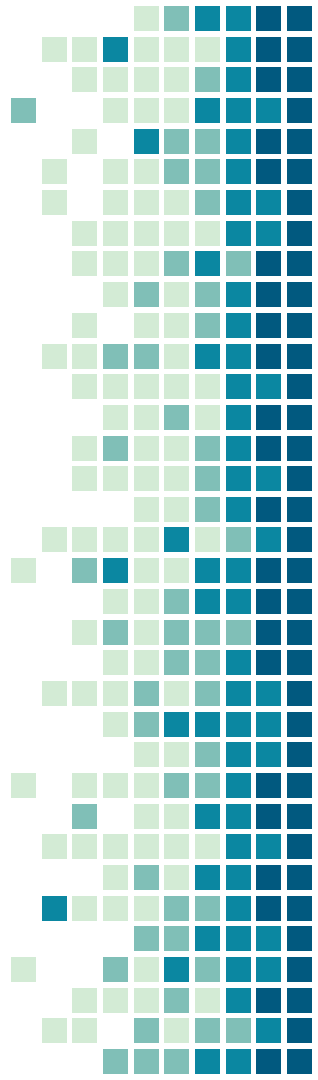
smoking



obesity

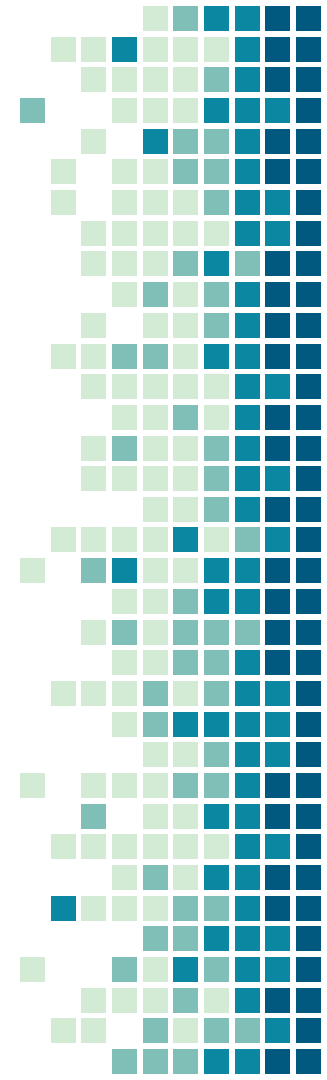
Causes of DVT

- Family history of clots
- Sitting for too long without moving such as long haul flights, travel, bed rest
- Having a long-term catheter
- Obesity
- Surgeries, recent fractures in the hips, pelvis or legs

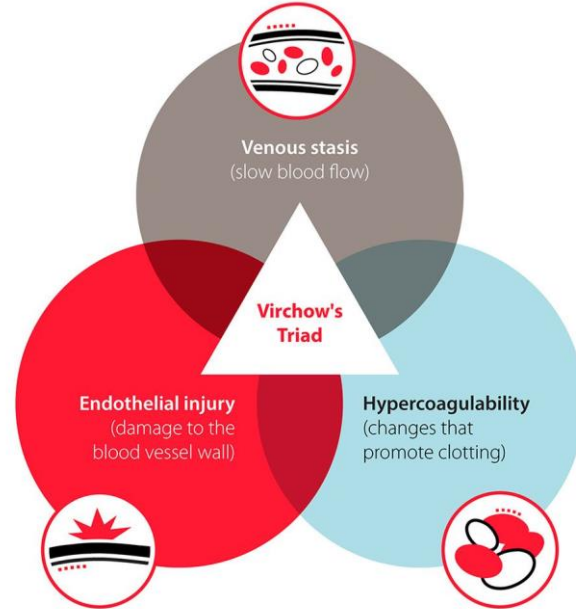


Symptoms of DVT

- Swelling in the calf (lower leg) or thigh
- Painful leg, tenderness in the leg (gets worse when you have to exert weight on it)
- Veins in the leg looking swollen or bulging
- Skin feeling warm and looking purple or red.

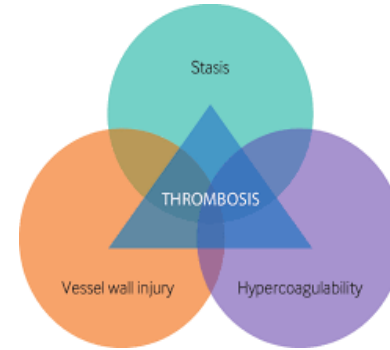


Credits to the famous Virchow's Triad to help diagnose formation of venous thrombosis



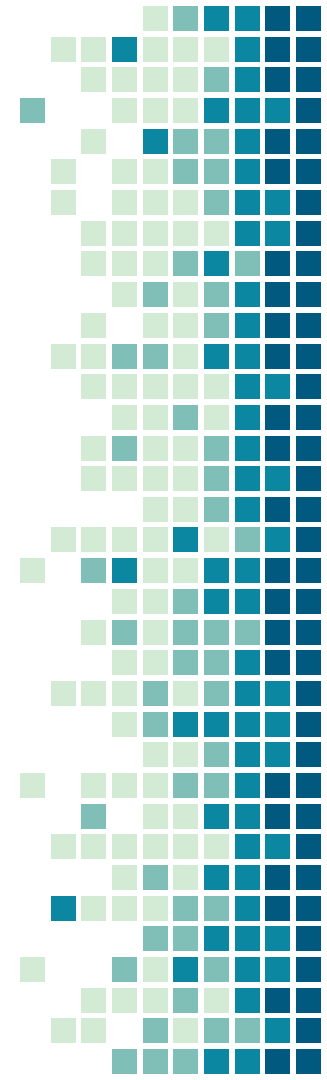
Virchow's Triad and its three components

- Stasis or interruption of the blood flow. Includes changes and alterations in blood flow due to various situations.
- Injury to the blood vessel walls. Piercing of blood vessel, shear stress, hypertension are certain ways of how the epithelial layer of the blood vessel can get damaged.
- Hypercoagulation of blood/ hypercoagulability is the formation of blood clot due to changes in the molecular structure of blood or genetic factors.
- Virchow's Triad plays a crucial role in the genesis of DVT.



Diagnosis of DVT

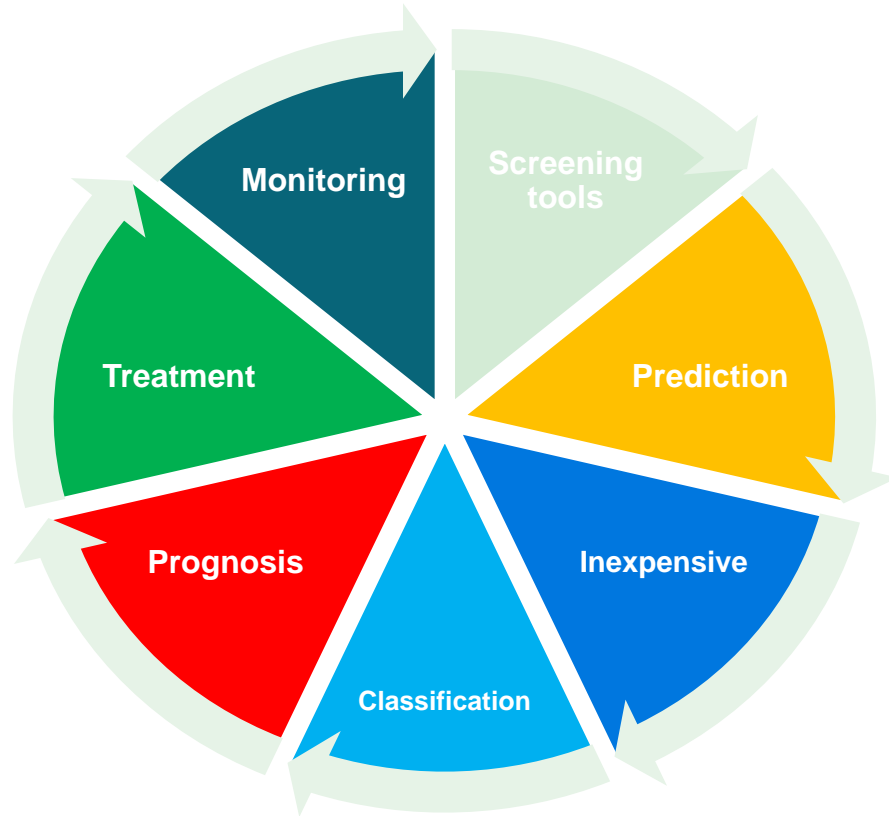
- Blood Tests
- Ultrasound tests
- CT scans
- MRI imaging
- Doppler imaging



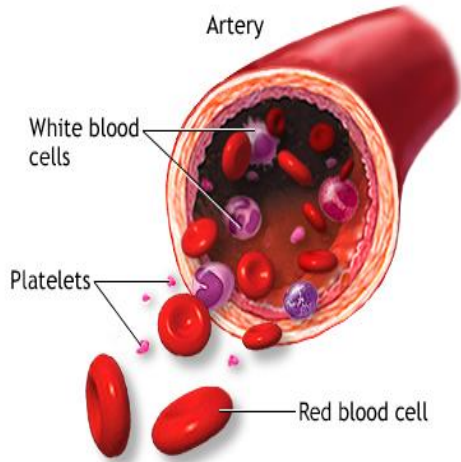
Blood Tests – used to determine the count of cellular indices



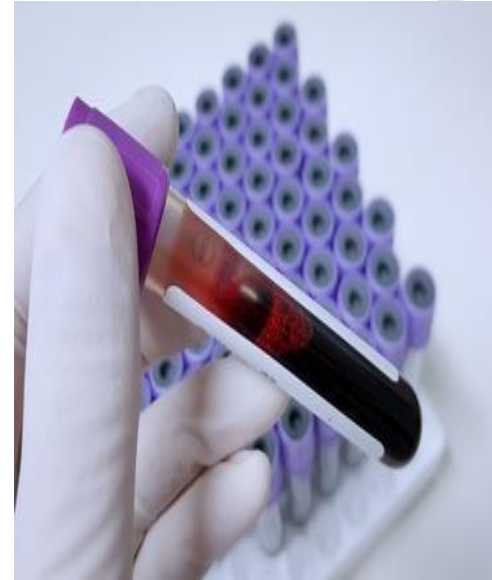
Blood cellular indices - indicators



Routine Complete Blood Count (CBC)

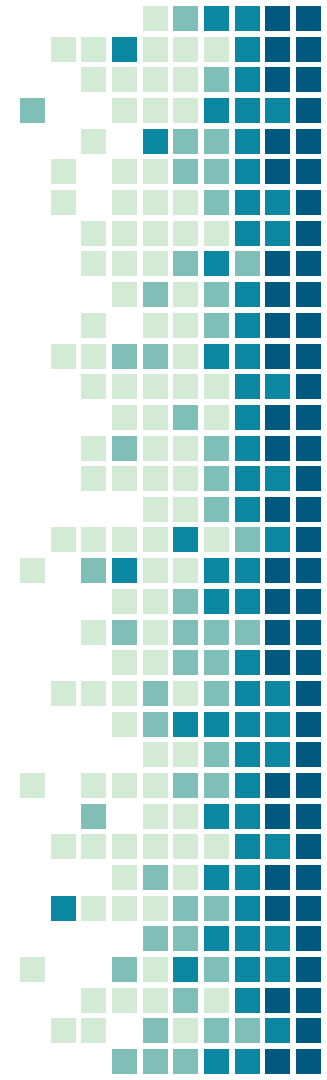


- CBC is a routine and inexpensive laboratory test performed in all Hematology laboratories.
- Bloods are collected in EDTA sample tubes and is tested on Hematology analysers, which provides information on it's the three main constituents of blood
 - RED BLOOD CELLS (RBC)
 - WHITE BLOOD CELLS (WBC)
 - PLATELETS



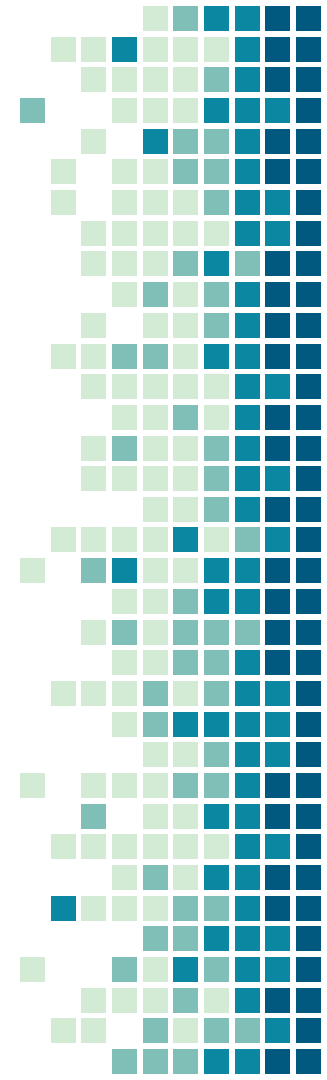
Evaluation of CBC parameters for predicting DVT

- RBC indices
- WBC subtypes and ratios
- Platelet indices

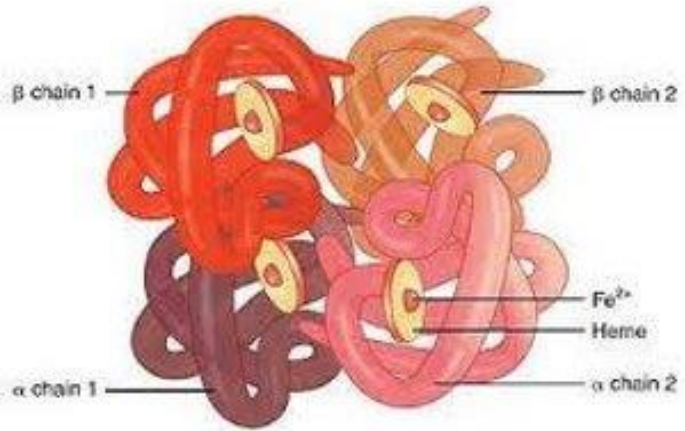


Red Cell Indices

- Hemoglobin (HGB)
- Hematocrit (HCT)
- Mean Platelet Volume (MPV)
- Platelet Count
- Red Cell Distribution



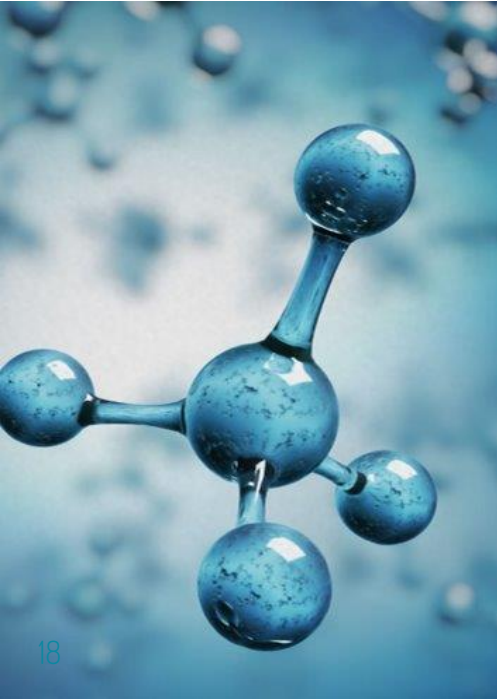
Hemoglobin

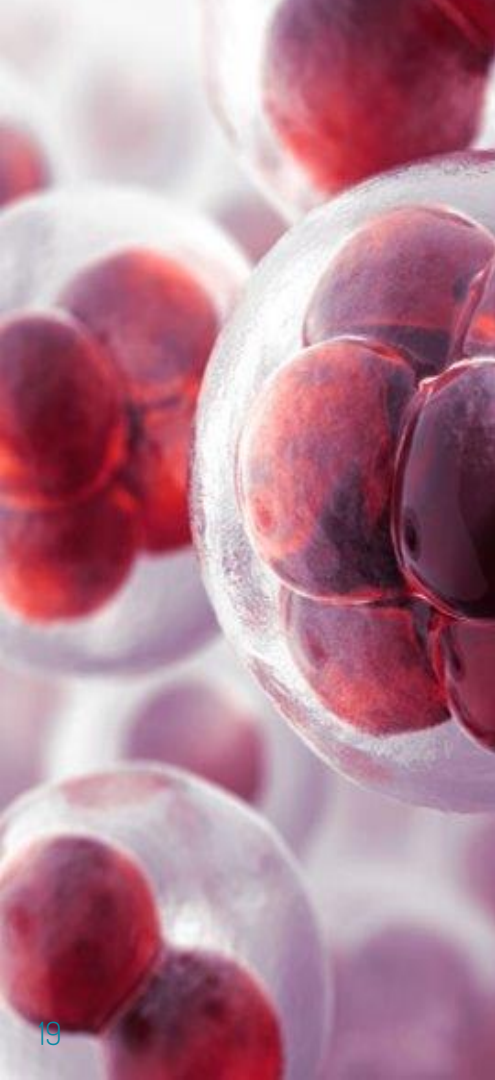


- Hemoglobin is a protein which is used to transport oxygen in human blood.
- Molecule for hemoglobin has 4 subunits each housing an iron atom bound to a heme group
- Low rates of hemoglobin are shown to relate to higher mortality rate for patients with Pulmonary Embolism
- This indicator for thrombosis has a roughly 74% accurate reading for whether a person has thrombosis
- Less than 11.15g/dl for hemoglobin was the cutoff for likelihood of PE or death by PE

What is Hemoglobin?

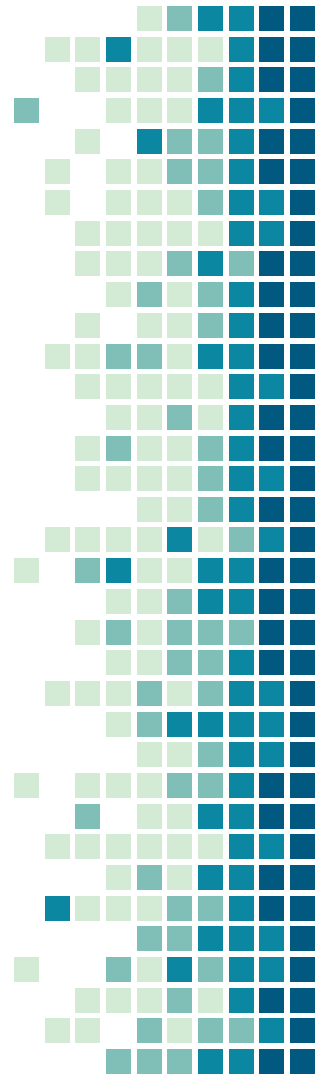
- Hemoglobin is a globular protein present in RBCs.
- It is a tetrameric protein which develops in the bone marrow, containing a heme prosthetic group attached to each subunit.
- **α** subunit – consists of alpha polypeptide chain containing 141 amino acid residues.
- **β** subunit – consists of beta polypeptide chain containing 146 amino acid residues.
- These are the normal hemoglobin levels for these age ranges:
 - Newborn – 17-22 g/dl
 - Children – 11-13 g/dl
 - Adult male – 14-18 g/dl
 - Adult female – 12-16 g/dl
 - Old males – 12.4-14.9 g/dl
 - Old females – 11.7-13.8 g/dl





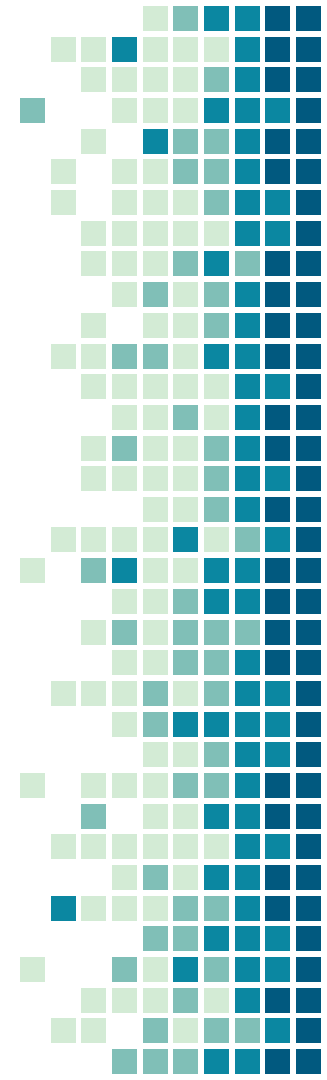
Hematocrit

- Hematocrit is the proportion of red cells to volume in the blood, or the density of red cells in the blood
- The cutoff for determining whether there is a probability of having thrombosis or the risk of mortality is having less than 34.15g/dl for Hematocrit
- Reference intervals for hematocrit are higher in men than in women however, which must be considered
- The study used for this showed that, very similar to Hemoglobin, lower values for Hematocrit correlated directly to higher mortality rates in thrombosis patients



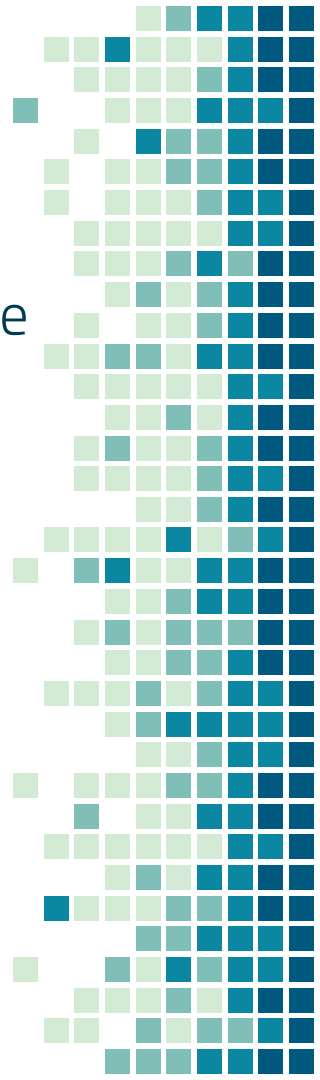
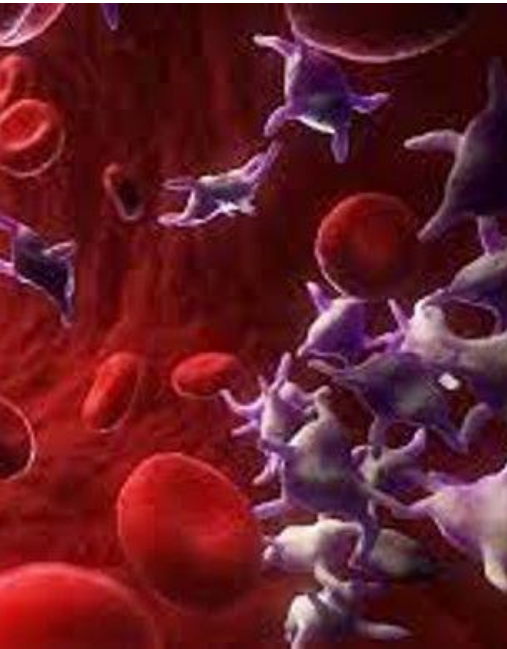
Platelet Count

- Thrombocytopenia is caused by low platelet count or destruction of platelets after they are formed. When platelet count falls below 10,000 platelets per microliter, fatal bleeding can occur
- Thrombocytosis however is caused when there are excessive platelets being produced
- This can lead to thrombocythemia which can cause different complications involving thrombosis. Including: Stroke, Myocardial Infarction (Heart Attack)



Mean Platelet Volume

- MPV is the average size of platelets in the blood
- Platelets vary in size, & larger platelets are much more reactive and have a greater chance of causing thrombosis
- This leads to a higher value for MPV causing a higher risk for DVT and Myocardial Infarction (Heart Attack), as well as for VTE



Red Cell Distribution Width

- Red cell distribution, if shown to be irregular, is a sign for thrombosis, as having high RDW in one area of the body while low in another may signal that a clot is blocking blood flow from one part of the body to another.



Hematology, Transfusion and Cell Therapy

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Original article

Serial values of hematologic variables and deep venous thrombosis: Red cell distribution width is associated with deep venous thrombosis

Govind R. Patel [ORCID](#), Manoranjan Mahapatra, Sadhna Aggarwal, Renu Saxena

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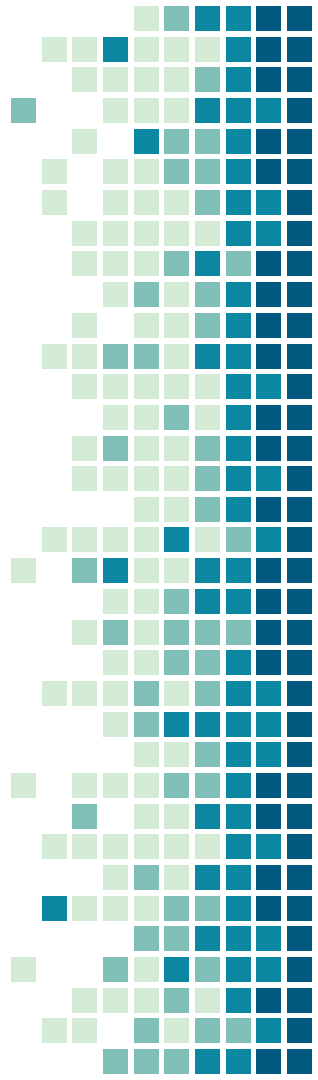
<https://doi.org/10.1016/j.htct.2022.11.005>

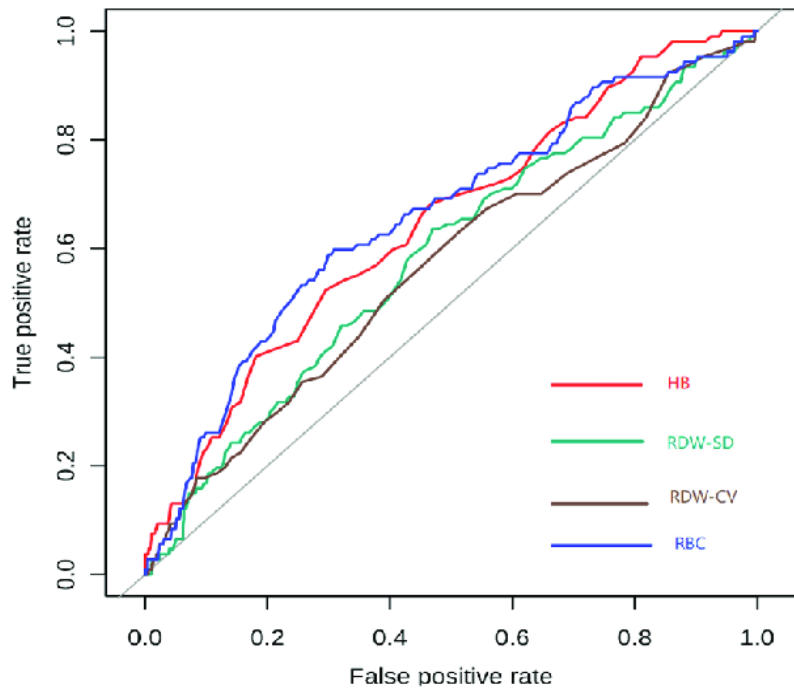
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This study evaluated association between serial values of hematologic variables and DVT. The study demonstrated a consistent association of high RDW value in first episode of DVT in patients.

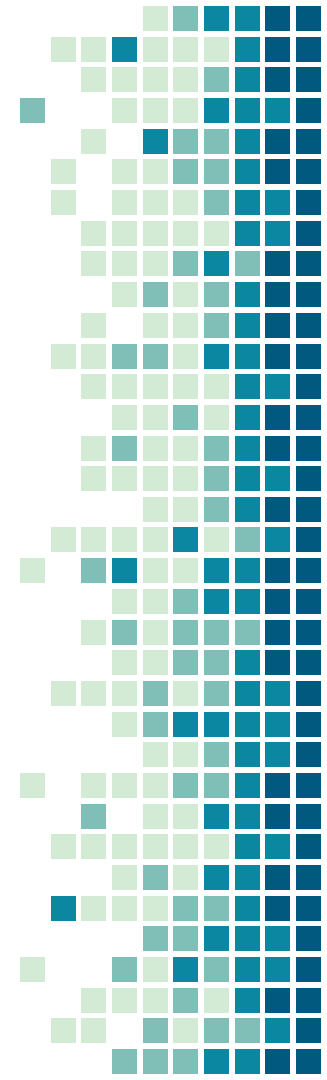




Maker	Cut off value	P-value	sensitivity	specificity	AUC	95% CI
RBC($10^9/L$)	3.92	0.001	70%	50%	0.658	0.6-0.712
Hb(g/L)	118	0.027	70%	50%	0.646	0.59-0.701
RDW-CV(%)	13.2	0.018	60%	50%	0.568	0.512-0.625
RDW-SD(fL)	44.6	0.003	50%	60%	0.586	0.531-0.64

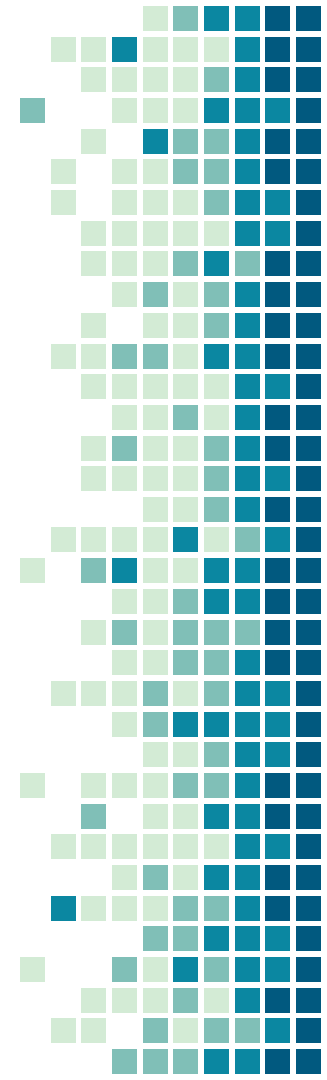
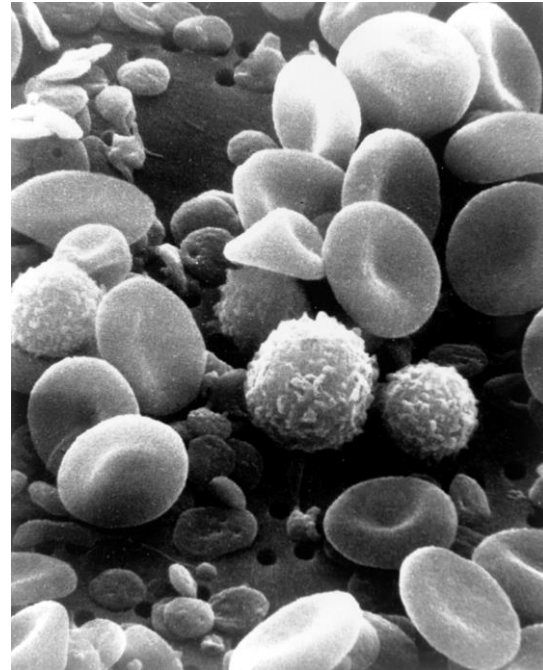
Diagnostic performances of RBC, Hb, RDW-CV and RDW-SD for prediction of DVT. Abbreviations: AUC: area under curve; CI: confidence interval; RBC: red blood cell; Hb: Hemoglobin; RDW-CV: red cell distribution width-coefficient of variation; RDW-SD: red blood cell-standard deviation; $P < 0.05$ was statistically significant.

Adapted from (Xiong et al., 2022)



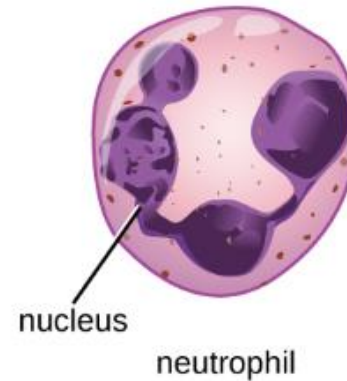
White Cell Indices

- Neutrophils
- Lymphocyte
- Neutrophil Lymphocyte Ratio (NLR)
- Platelet Neutrophil Ratio (PNR)
- Monocyte Neutrophil Ratio (MNR)
- Eosinophils
- Basophils



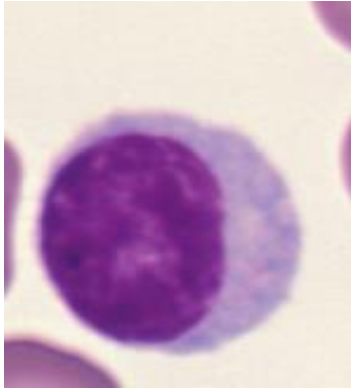
Neutrophils

- White blood cell which initiates the immune response
- "First Responders"
- Destroy viruses by ingesting them
- Additionally, boost response of other cells
- Studies found that depletion of neutrophils prevents venous thrombus
- Release of NETs.



Adapted from (Cellular defenses)

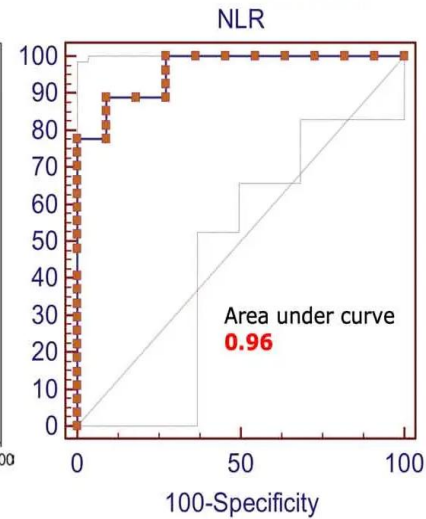
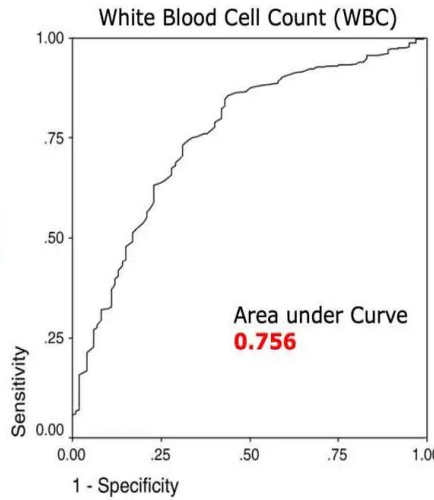
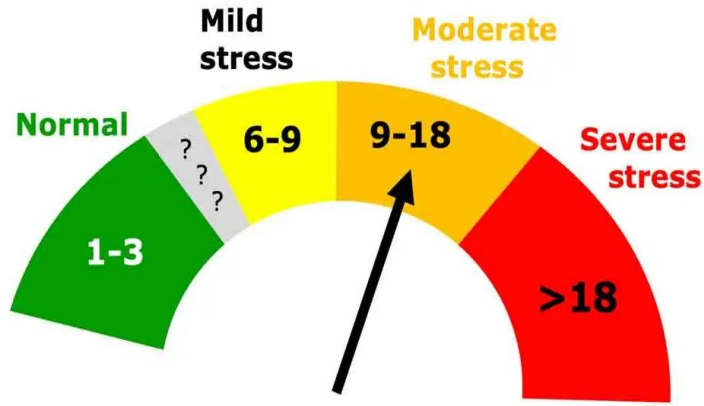
Lymphocytes



Adapted from (Pathology outlines)

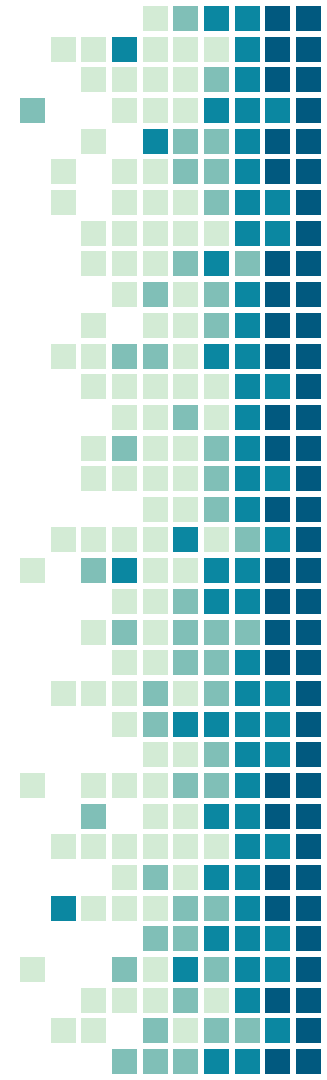
- Immune cell made in bone marrow
- 2 main types
- B – Produce antibodies which bind to proteins
- T – Kill tumor cells and control immune response
- Antibodies from B cells can clear foreign pathogens, but may also damage the healthy cells
- For DVT, this system may lead to the activation of platelets
- A mouse model showed that blocking the activity of the cytokines could reduce the severity of DVT

NLR Stress-o-Meter

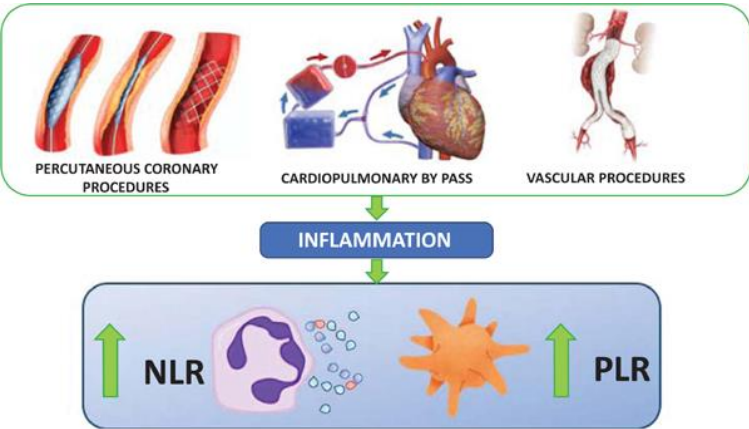


NLR

- Neutrophil Lymphocyte Ratio
- Inexpensive blood test
- An elevated NLR is a sign of inflammation
- High NLR has shown to be associated with re-occurrence of DVT.
- Possible promising tool for diagnosis



PNR

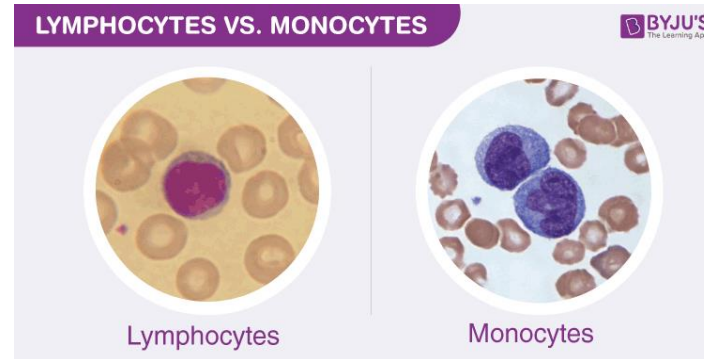


Neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio as biomarkers for cardiovascular surgery procedures.

- Platelet Neutrophil Ratio
- Measures the ratio of platelets to neutrophils
- Newer biomarker
- Elevated PNR is associated with inflammation and can be used as a predictor of poor outcomes
- Not specific and needs to be used with other tests

LMR

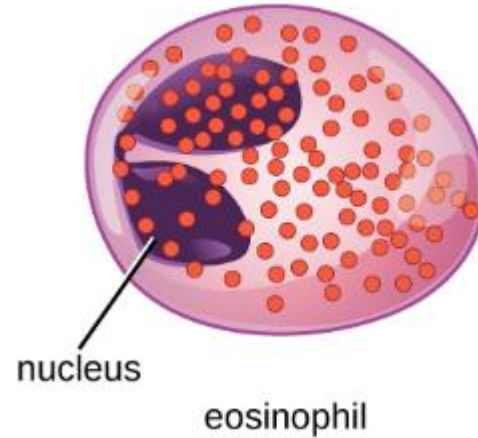
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Adapted from Byjus

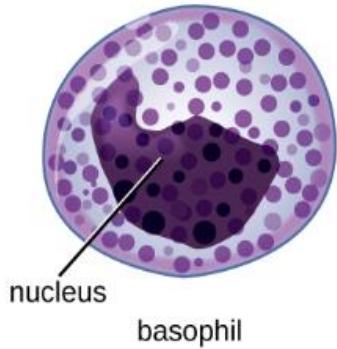
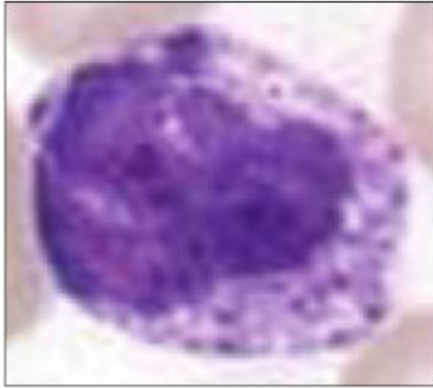
Eosinophils

- Specialized immune cells with enzymes released during infections
- Allergies (Hay Fever)
- Characterized by granules in cytoplasm
- Measured as part of a CBC
- Not used to diagnose DVT



(Adapted from Cellular defenses)

Basophils



- Response to allergens
- Filled with histamine
- Research has indicated that Basophil activation is inflammatory response after formation of DVT
- The process of basophils releasing histamine can cause swelling

(Adapted from Cellular defenses)

Doctors Fakiha Siddiqui and Jaweed Fareed et al

Table 1.

Mean Values At Baseline Of The 3 Cellular Indices, According To The Clinical Characteristics Of The Patients.

	N	Neutrophil Count	Lymphocyte Count	Platelet Count	NLR	PLR	SII
Clinical characteristics,							
All patients	4487	7.7 ± 8.2	2.0 ± 3.1	246 ± 104	5.9 ± 7.1	190 ± 158	1459 ± 2028
Female sex	2115	7.7 ± 8.7	2.1 ± 3.1	255 ± 104 [‡]	5.5 ± 6.6 [‡]	189 ± 147	1410 ± 1888
Age >70 years	1956	7.5 ± 7.7	1.8 ± 2.8 [‡]	232 ± 98 [‡]	6.3 ± 6.9 [‡]	195 ± 154	1470 ± 1831
Body weight <70 kg	1425	7.7 ± 8.3	1.9 ± 3.1	255 ± 115 [‡]	6.3 ± 7.8 [†]	210 ± 179 [‡]	1626 ± 2308 [‡]
Risk factors for VTE,							
Active cancer	715	7.2 ± 7.7	1.8 ± 3.5*	252 ± 131	6.4 ± 7.4*	230 ± 196 [‡]	1687 ± 2402 [†]
Recent surgery	381	7.5 ± 6.5	1.9 ± 2.5	295 ± 160 [‡]	5.6 ± 5.2	222 ± 164 [‡]	1687 ± 1844*
Immobility for ≥4 days	1384	8.0 ± 8.1	1.8 ± 2.7 [†]	254 ± 106 [‡]	7.2 ± 9.2 [‡]	221 ± 180 [‡]	1819 ± 2564 [‡]
Estrogen intake	210	9.1 ± 11.8	2.9 ± 4.7 [†]	263 ± 85*	4.4 ± 3.8 [‡]	160 ± 123 [‡]	1149 ± 1161 [‡]
Pregnancy/postpartum	37	8.8 ± 3.4	1.9 ± 1.2	287 ± 104*	5.6 ± 3.6	197 ± 137	1738 ± 1682
Unprovoked	2067	7.5 ± 8.0	2.2 ± 3.1 [†]	230 ± 85 [‡]	5.0 ± 5.4 [‡]	160 ± 127 [‡]	1160 ± 1445 [‡]
Prior VTE	524	7.7 ± 9.2	2.4 ± 4.4*	230 ± 89 [‡]	4.9 ± 5.3 [‡]	161 ± 120 [‡]	1134 ± 1415 [‡]
Leg varicosities	695	7.3 ± 7.8	1.9 ± 2.0	232 ± 89 [‡]	5.3 ± 5.9 [†]	168 ± 132 [‡]	1242 ± 1630 [‡]

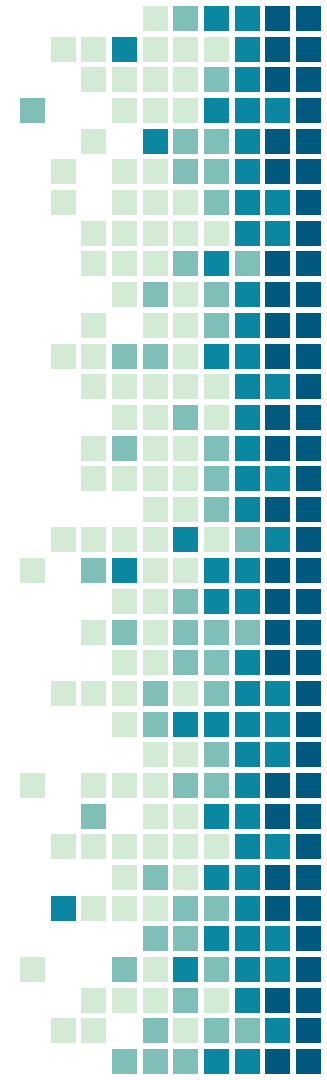
- RIETE database (Registro Informatizado de Enfermedad Tromboembolic) was used to determine the association between Neutrophils, Lymphocytes, and their ratios to VTE
- Patients with higher baseline NLR were at higher risk of major bleeding
- High SII (systemic immune inflammation) index values were at a risk for increased mortality
- In this study, patients gave consent for participation in the registry
- The parameters recorded in RIETE were the demographics, initial VTE presentation, clinical status, recent bleeding, risk factors for VTE, baseline blood tests, treatment received, and outcomes.
- Mean NLR and PNR values were higher in patients initially presenting with PE, and the lowest for patients with lower-limb DVT.
- SII Values were highest in patients with PE

Results support that none of the three baseline cellular indices were sufficient for prediction of VTE recurrences in acute VTE patients. The patients with higher baseline NLR values were at an increased risk of major bleeding or death, those with high SII values were at an increased risk for mortality.



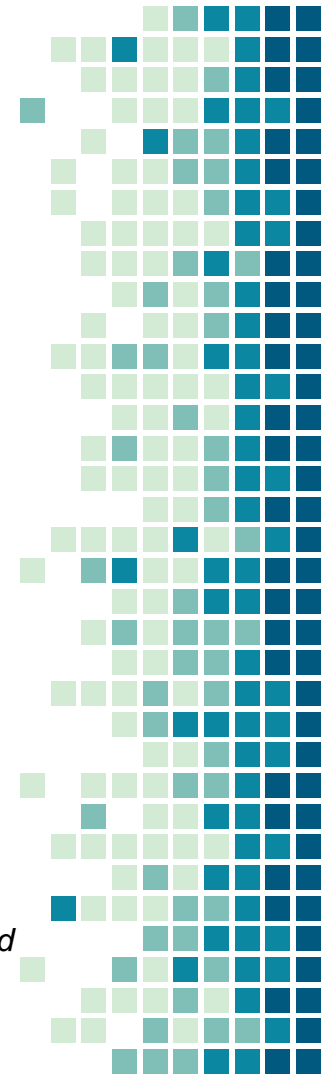
Conclusions

- Increased RDW and HCT are associated with patients suffering from DVT.
- Increased NLR is associated with a higher risk of DVT re-occurrence.
- These cellular indices could serve as better indicators or diagnostic tools and prognostic markers for DVT.
- Complete blood count data is routinely obtained in emergency and in-patient settings. It is a widely used, low-cost, convenient laboratory test that offers an abundance of metrics
- These readily available blood cellular indices along with other testing strategies can help accurate diagnosis in a timely manner.



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Acknowledgements

We are extremely grateful to our mentor Neha Thomas and Dr. Atul Laddu for their invaluable guidance, expertise, and unwavering support throughout this research project. Their mentorship made a significant benefit in the development and execution of this project.

