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Deciphering Endothelial and Coagulation Disturbances in Patients with Acute Myeloid Leukemia at High Risk of Early Complications

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INTRODUCTION

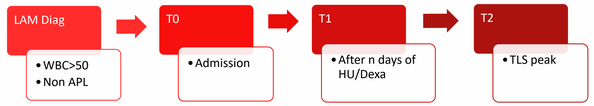
Acute myeloid leukemia with high hyperleukocytosis (HL-AML) is associated with a 15-20% risk of early organ-failures and mortality mainly owing to pulmonary or other organ hemorrhages associated with leukostasis or specific infiltration. The risk of life-threatening complications is found in all subgroups of AML. Disturbances in endothelial function or coagulation abnormalities may be involved, but this has never been studied in a comprehensive manner.

AIM

In this study, we aimed to perform a multiparametric analysis of all areas of coagulation and endothelial function in patients with HL-AML to find a relation with the risk of life-threatening complications.

METHOD

- Mono-centric prospective exploratory non-interventional study
- Inclusion / Exclusion
  - Adult patient with AML and leukocytes > 50G/L
  - Exclusion of patients with AML3 or prior treatment or relapse
  - Exclusion of patients with past history or treatment modifying hemostasis
- 40 patients to be included (initially planned over two years.)
- Prospective plasma banking at different time points
- Principal component analysis to identify homogeneous groups of coagulation/endothelial disturbance profile



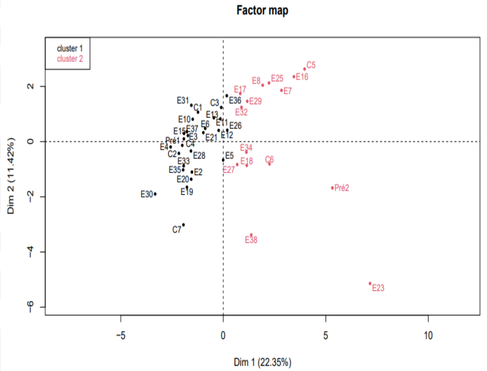
RESULTS

47 patients were included between september 2018 and august 2022

Parameters	Variable	N	Statistics
		47	Total
Age		47	57 [44;64] (28;79)
Sex	Men	31	66 %
	Women	16	34 %
Medical history			
	Cardiovascular	9	19 %
	Obésité	3	6 %
	Respiratory	1	2 %
	Kidney disease	1	2 %
FAB	4	20	45 %
	5	12	27 %
	Other	15	28 %
Oxygen	Oui	18	38 %
	Non	29	62 %
Leucocytes (G/ L)		47	85.3 [55;134] (2.67;542)

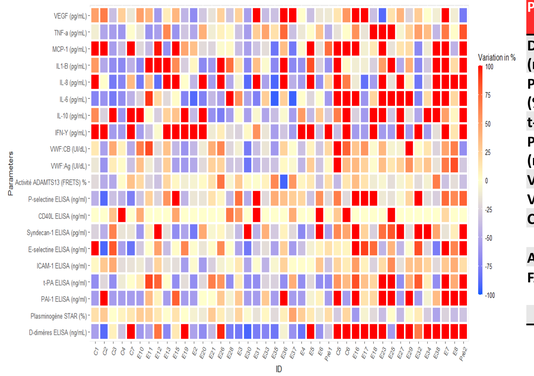
Cluster 1:

- **High values for the variable Plasminogen**
- **Low values for the variables D-dimer, VWF:Ag, ICAM-1, Syndecan-1, VWF:CB, t-PA, sVCAM-1, E-selectin, IL-6 and PAI-1**



Cluster 2:

- **Low values for the variable Plasminogen**
- **high values for the variables D-dimer, VWF:Ag, ICAM-1, Syndecan-1, VWF:CB, t-PA, sVCAM-1, E-selectin, IL-6 and PAI-1**



Clinically relevant events: haemorrhagic events including respiratory failure with IOT

-> 21 events

Paramètres	Valeurs	N	Nevent	OR	IC95%	p-value
D-dimères ELISA (ng/mL)		42	21	1,23	(1.01 - 1.49)	0,039
Plasminogène STAR (%)		42	21	0,96	(0.93 - 0.99)	0,015
t-PA ELISA (ng/ml)		42	21	1,01	(0.99 - 1.23)	0,075
P-selectine ELISA (ng/ml)		42	21	1,02	(1 - 1.04)	0,037
VWF:Ag (UI/dL)		42	21	1,13	(1.04 - 1.22)	0,003
VWF:CB (UI/dL)		42	21	1,09	(1.01 - 1.17)	0,022
Cluster	Cluster 1	27	9	1,00		
	Cluster 2	15	12	8	(1.79 - 35.75)	0,006
Age		42	21	1,04	(0.99 - 1.09)	0,10
FAB 4/5	Autres FAB	12	3	1,00		
	FAB 4/5	30	18	4,5	(1.01- 20.11)	0,049

CONCLUSIONS / PERSPECTIVE

→ **2 clusters of patients not identifiable on standard clinical or biological criteria are identified on admission**

Cluster 2 comprises 15/42 patients

- **corresponds to homogeneous activation of coagulation, platelet fibrinolysis and endothelium**
- **No association with patient characteristics / AML**
- **Strong, independent association with the occurrence of life-threatening distress, with an odds ratio of 8**

→ **Future direction : Understanding how to decrease the risk in this context with use of Hydroxyurea first before chemotherapy and dexamethasone**

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