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Supplementary Table 1. Summary of the studies reporting unchanged and changed platelet phenotypes due to chronic kidney disease

Study (N)	Study group	Control group	Platelet test	Findings
A.Unchanged phenotype				
Dudley (N=21)	Dogs with CKD	Dogs without CKD	Closure time on PFA-100 analyzer	No difference in closure time between CKD and control dogs
Forsythe (N=47)	Dogs with CKD	Dogs without CKD	Impedance aggregometer	No difference in whole blood platelet aggregation induced by collagen, ADP and arachidonic acid
Ho (N=42)	Patients with CKD with a GFR of <30ml/ min with or without dialysis	None	Bleeding time, aggregation measured by PFA-100 and cone analyzer	No correlation between bleeding time and aggregation measurements using various approaches
Zwaginga (N=10)	Patients on hemodialysis	None	Optical aggregometer	Normal aggregation
Mourikis (N=22)	Patients on chronic hemodialysis with CAD	None	Optical aggregometer	No difference in platelet aggregation 2 hours after hemodialysis vs that before treatment
Gackler (N=50)	Patients on chronic dialysis and few non-dialysis CKD	Healthy controls	PFA-100, multiple electrode aggregometer	No difference in platelet aggregation in CKD patients
Ballard (N=28)	Chronic uremia patients not on dialysis	Healthy young adults	Optical aggregometer	No difference in ADP induced platelet aggregation between groups
Zeck (N=10)	CKD stage 4-5 patients not on dialysis	None	Whole blood platelet aggregometer and ATP release by agonists	No abnormalities detected in platelet aggregation and ATP release
Mavrakana (N=771)	Patients with known stable CAD, CVA or PVD	None	PFA-100 analyzer	No difference in platelet aggregation between participants with GFR values ≥60 ml/min/1.73m^2 vs. those with <60 ml/min/1.73m^2
Kim (N=1,716)	Patients admitted to a hospital	None	Whole blood PFA-100 analyzer	No correlation of bleeding time with GFR
Huang (N=115)	Patients with CKD stages 3-5	Healthy controls	Optical aggregometer	No differences in platelet aggregation between groups

Jain (N=44)	Patients with stages 4-5 CKD	Healthy controls	Whole blood platelet aggregometer	No major differences in platelet aggregation and ATP secretion between groups
B. Changed phenotype				
Rabiner (N=18)	Chronic hemodialysis patients	None	Optical aggregometer	Elevated levels of phenolic acid derivatives induced platelet aggregation abnormalities that corrects with hemodialysis.
Sloand (N=30)	Chronic hemodialysis patients receiving dialysis	Chronic hemodialysis patients not dialyzed for the last 48 hours and receiving heparin infusion	Optical aggregometer and bleeding time	No difference in ADP induced platelet aggregation between groups, with reduced thrombin and ristocetin induced platelet aggregation;
Gawaz (N=18)	Patients on hemodialysis	Healthy controls	Flow cytometry	Increase in bleeding time which improved with dialysis treatment Glycoprotein IIb/IIIa on the platelet surface is unable to undergo conformational change upon ADP activation in CKD patients
Pluta (N=30)	Patients on chronic hemodialysis on transplant waiting list	Healthy volunteers	Whole blood impedance aggregometer	Lower platelet activity in dialysis patients compared to the controls
Mekawy (N=60)	Patients on chronic hemodialysis	Healthy controls	PFA-100 analyzer	Prolonged closure time in hemodialysis patients improved with hemodialysis treatment.
Ando (N=118)	Patients with and without dialysis	Healthy controls	Platelet microparticles by flow cytometry	Platelet microparticles were higher in plasma of patients with CKD
Sreedhara (N=111)	Patients with CKD including those on hemodialysis	Healthy controls	Shear induced platelet aggregation; flow cytometry measurements for platelet surface receptors	CKD patients had reduced platelet aggregation, and reduced surface expression of glycoprotein IIb/IIIa protein.
Moal (N=107)	Patients on hemodialysis, and non-dialysis patients	Healthy controls	Optical aggregometer	Bleeding time was increased in patients with CKD. ADP and arachidonic induced

				platelet aggregation was normal in the two groups. Ristocetin induced aggregation was increased in patients with CKD.
Zhu (N=6,745)	Patients with CKD 3-5 undergoing PCI	Patients with CKD 1-2	Modified thromboelastography (mTEG) test in whole blood	High residual ADP aggregation, defined as ADP inhibition <30% on aspirin and clopidogrel, in patients with more severe CKD

Abbreviations: ADP-adenosine diphosphate, ATP-adenosine triphosphate, CAD-coronary artery disease, CKD-chronic kidney disease, CVA-cerebrovascular accident, GFR-glomerular filtration rate, PFA-platelet function analyzer, PVD-peripheral vascular disease.

Supplementary Table 2. Summary of studies reporting platelet phenotype for bleeding complications in patients with chronic kidney disease

Study	Study group	Control group	Platelet test	Findings
Castaldi (N=19)	CKD and acute kidney injury patients **with** bleeding events	CKD and acute kidney injury patients **without** bleeding events	Optical aggregometer	No difference in platelet aggregation between groups
Di minno (N=20)	Patients undergoing chronic hemodialysis, peritoneal dialysis or pre-dialysis with prolonged bleeding time	Healthy controls	Optical aggregometer and ATP release	ADP induced aggregation was high and ATP release to collagen was reduced in CKD vs. controls
Horowitz	Samples from uremic patients		Optical aggregometer	ADP induced platelet aggregation was lower in uremic patients due to the presence of guanidinosuccinic acid in uremic plasma
Eknoyan (N=36)	Patients with CKD not on dialysis, stratified by bleeding events	Healthy controls	Platelet binding to von Willebrand factor	Ability of platelet to bind to von Willebrand factor was reduced in CKD patients with bleeding events compared to those without bleeding events
Remuzzi (N=60)	Patients receiving hemodialysis	Healthy controls	Bleeding time	Bleeding time was prolonged in dialysis patients, without any correlation to biochemical parameters

Abbreviations: ADP-adenosine diphosphate, ATP-adenosine triphosphate, CKD-chronic kidney disease

Supplementary Table 3. Summary of studies reporting effects of uremic toxins on platelet function

Study	Study group	Control group	Platelet test	Findings
Yang	C57BL/6J mice		Flow cytometry and optical aggregometer	Indoxyl sulfate increases P-selectin and glycoprotein IIb/IIIa expression on the platelet surface in a dose-dependent manner.
Chang	Platelet isolates from rabbits and humans	Exposed ex vivo to p-cresol (uremic toxin) or sham	Optical aggregometer	p-cresol resulted in antiplatelet effects with the inhibition of arachidonic acid induced platelet aggregation.
Karbowska	Wistar rats	Infused with indoxyl sulfate or sham	Optical aggregometer	Indoxyl sulfate resulted in dose-dependent increase in collagen induced platelet aggregation
Bazilinski	Uremic plasma from patients on hemodialysis with bleeding complications		Optical aggremometer	Platelet aggregation was inhibited
Davis	Uremic plasma of patients on chronic hemodialysis	Addition of urea and GSA ex vivo to plasma	Optical aggregometer	ADP induced platelet aggregation was reduced with urea but not with GSA

Abbreviations: ADP-adenosine diphosphate, GSA-guanidinosuccinic acid