MECHANISMS OF CEREBRAL MICROVASCULAR DISEASE IN CKD

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CKD AND CEREBRAL MICROVASCULAR DISEASE

• CLINICAL OBSERVATIONS
• EPIDEMIOLOGY
• CALCIFICATION & ERYTHROPHAGOCYTOSIS
• MICROVASCULAR CONSIDERATIONS
  • ANIMAL (IN VIVO) MODELS: INDUCTION OF MICROHEMORRHAGE
  • CELL CULTURE (IN VITRO) MODELS: IMPACT OF UREA
  • MICROBIOME-DERIVED UREMIC TOXINS
CEREBRAL MICROVASCULAR DISEASE

• ISCHEMIC
  • SMALL, DEEP INFARCTS/LACUNES
  • MICROINFARCTS
  • WHITE MATTER DISEASE/HYPERINTENSITIES/LEUKOARAIOSIS
• HEMORRHAGIC
  • MICROBLEEDS/MICROHEMORRHAGES
• OTHER
  • ATROPHY

PROGRESSION OF CEREBRAL MICROBLEEDS IN A HEMODIALYSIS PATIENT

(Li et al Hemodialysis International 2015)
PROGRESSION OF MICROBLEEDS IN HEMODIALYSIS

(Lau et al Transl Stroke Res 2019)

(Cystatin C and Risk for Dementia

(Cystatin C and Microvascular Disease

(Lau et al Neurobiology Aging In Press)
MECHANISMS OF CEREBRAL MICROVASCULAR DISEASE IN CKD

(Lau, Huisa, Fisher Transl Stroke Res 2017)

ARTERIAL/ARTERIOLAR CALCIFICATION AND MICROVASCULAR DISEASE

INTRACRANIAL CALCIFICATION PREDICTS MICROBLEED LOAD
(Cho et al Diagnostics 2020)
ERYTHROPHAGOCYTOSIS AS A MICROBLEED MECHANISM?

(Chang et al Front Cell Neurosci 2018)

MICROHEMORRHAGES IN MOUSE MODEL OF CKD

CKD MOUSE MODELS

(Lau et al Transl Stroke Res 2019)

MICROHEMORRHAGES IN CKD MODEL INDEPENDENT OF BP
EFFECTS OF CKD SERUM AND UREA IN BBB MODEL

(Lau et al Transl Stroke Res 2019)

SUMMARY

• CLINICAL AND EPIDEMIOLOGY EVIDENCE LINKING CKD AND MICROVASCULAR DISEASE

• CEREBRAL MICROHEMORRHAGE INDUCTION IN CKD MOUSE MODEL INDEPENDENT OF BP

• UREA-INDUCED ENHANCED PERMEABILITY IN VITRO BBB MODEL

• MICROBIOME-DERIVED UREMIC TOXINS LIKELY CONTRIBUTE
CONCLUSIONS

MULTIPLE PLAUSIBLE MECHANISMS LINKING CKD WITH MICROVASCULAR DISEASE AND COGNITIVE DECLINE

EVIDENCE VARIES FROM CIRCUMSTANTIAL EXTRAPOLATIONS TO DIRECT IN VIVO AND IN VITRO EXPERIMENTAL STUDIES

QUESTION: IS VASCULAR COGNITIVE IMPAIRMENT SUBSTANTIALLY MEDIATED BY RENAL FUNCTION?

ACKNOWLEDGEMENTS

• UCI NEPHROLOGY: WEI LIN LAU, ANE NUNES, HAN LIU, NICK VAZIRI, KAM KALANTAR
• UCI MIND: DAVID CRIBBS
• UCI NEUROLOGY: ANNLIA PAGANINI-HILL, CLAUDIA KAWAS, MARIA CORRADA, DANA GREENIA, CHUO FANG
• UCI BECKMAN LASER INSTITUTE: BERNARD CHOI, CHRISTIAN CROUZET, DANNY XIE
• UCI RADIOLOGY: DANIEL CHOW, DAVID FLORIOLLI, PETER CHANG
• KECK GRADUATE INSTITUTE: RACHITA SUMBRIA, JESSICA SUN