Extracellular acidosis accelerates bone resorption by enhancing osteoclast survival, adhesion, and migration.

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Acidic extracellular pH promotes osteoporotic bone loss by osteoclast activation. However, the change of osteoclastic cell behavior in acidosis-stimulated bone resorption process is unknown. We found that lowering extracellular pH induced an increase in the survival, adhesion, and migration of mature osteoclasts with a full actin ring, leading to enhanced pit formation on dentine slices. Acidosis upregulated osteopontin, which is an Arg-Gly-Asp (RGD) motif-containing matrix protein secreted from osteoclasts and acts as a common modulator for their survival, adhesion, and migration. A synthetic RGD peptide treatment blocked acidosis-induced osteoclast adhesion and migration, likely by competing with the RGD motif-containing extracellular matrix proteins for cell surface integrin binding. We finally observed that acidosis was associated with activation of osteoclast survival/adhesion/migration-related Pyk2, Cbl-b, and Src signals. Collectively, the findings indicate that extracellular acidosis stimulates bone resorption by extending osteoclast survival and facilitating osteoclast adhesion and migration.