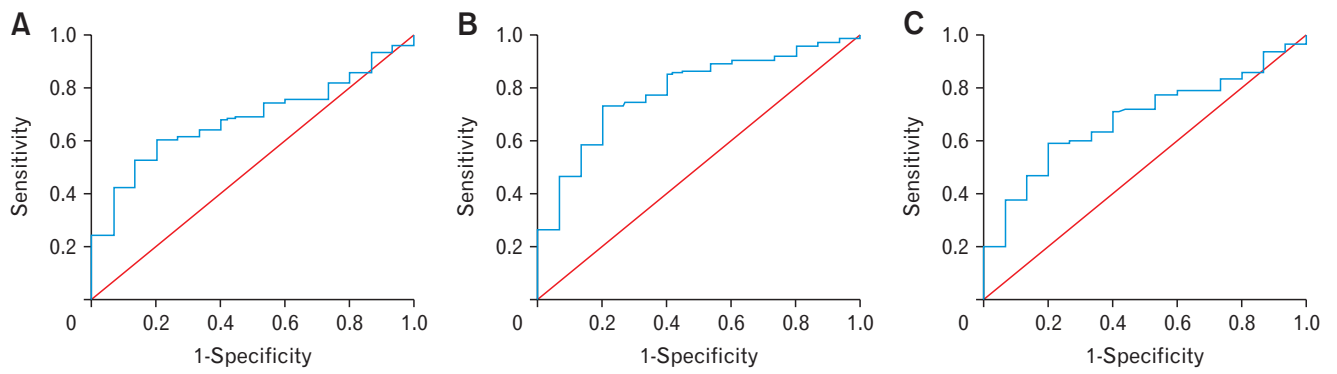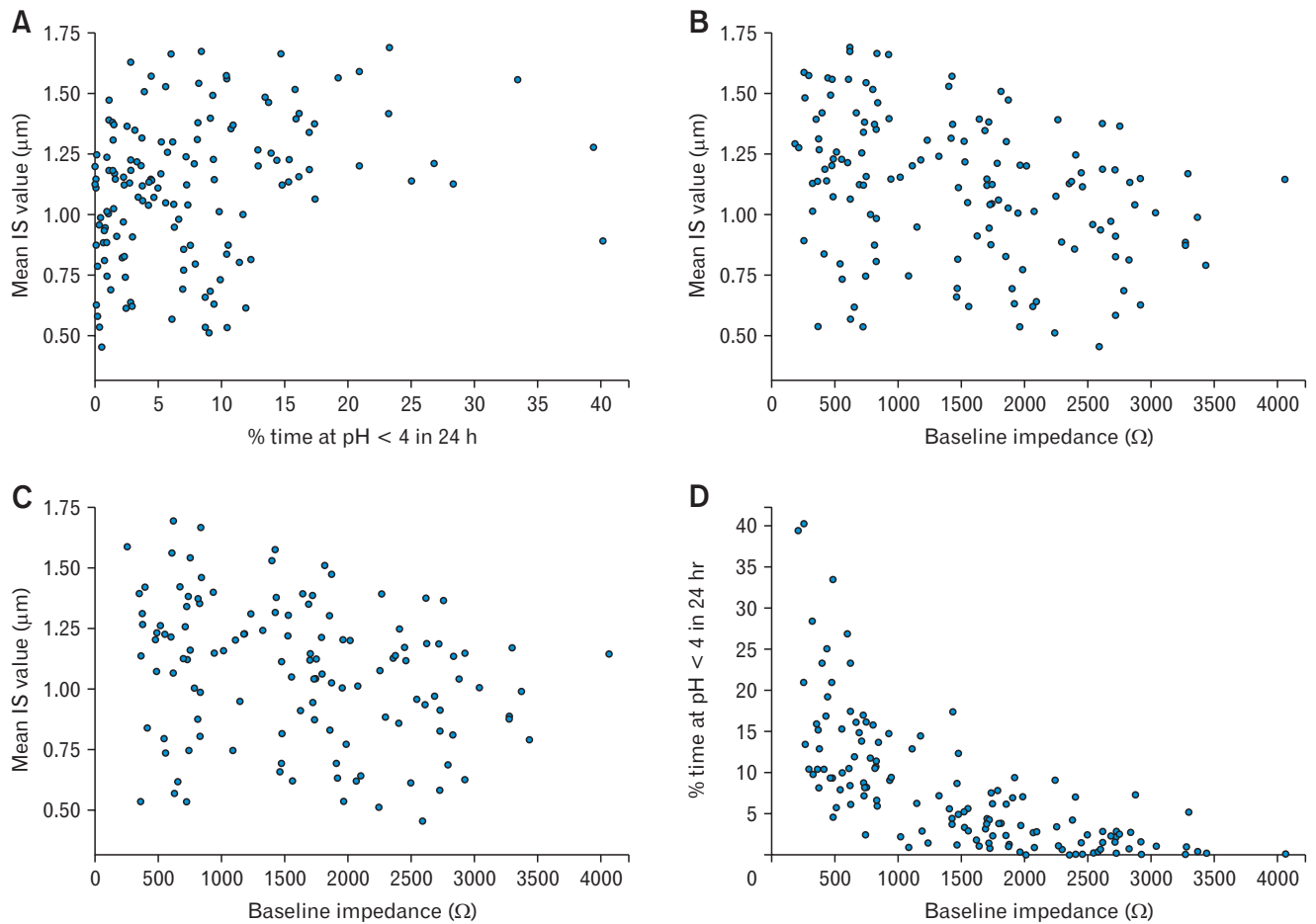**Supplementary Figure 1.** Representative images of intercellular space (IS) measurement. (A) Ten different hotspots were photographed for each specimen (200× magnification). (B) Ten perpendicular length measurements were performed around one epithelial cell that had the widest IS (the original 1000× magnification photograph was zoomed with software).

Supplementary Figure 2. Receiver operating characteristic curve analysis. (A) Healthy control (HC) vs acid exposure time > 6% (n = 78, area under curve [AUC] = 0.684, P = 0.024). (B) HC vs esophagitis in upper gastrointestinal endoscopy (n = 75, AUC = 0.790, P < 0.001). (C) HC vs all gastroesophageal reflux disease patients (n = 115, AUC = 0.684, P = 0.020).

Supplementary Figure 3. Scatter diagrams. (A) Mean intercellular space (IS) value and % time at pH < 4 in 24 hours (n = 141, Spearman's rho = 0.302, $P < 0.001$ two-tailed). (B) Mean IS value and baseline impedance (BI) (n = 140, Spearman's rho = −0.359, $P < 0.001$ two-tailed). (C) Mean IS value and BI without severe erosive reflux disease patients (n = 125, Spearman's rho = −0.296, $P = 0.001$ two-tailed). (D) % time at pH < 4 at 24 hours and BI (n = 138, Spearman's rho = −0.783, $P < 0.001$ two-tailed).