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Using Deep Convolutional Neural Networks to Automate Classification of Carotid Plaques from Ultrasound Imaging

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Background: Stroke is a devastating consequence of plaque rupture from the carotid arteries. Current management of carotid plaques involves waiting for symptoms (eg, stroke or ministroke); intervention itself has risk of stroke and not all plaques are vulnerable to rupture. There is a need to better risk-stratify plaque that causes stroke. Carotid ultrasound (US) examination is a noninvasive and inexpensive visualization of plaques, but is limited by human interpretation. We hypothesize that convolutional neural networks will identify unique features of carotid plaques for automated risk stratification.

Methods: Our workflow is illustrated in Figure *A*. A total of 141 B-mode US images of carotid arteries were included; 64 high-risk with symptomatic carotid plaques and 75 low-risk with no significant plaque. Data were cropped and divided into training (70%) and holdout test (30%) subsets. During model training, an ensemble of ResNet-18 convolutional neural networks learned classification of low-risk and high-risk cases using five-fold stratified cross-validation and was used to predict on the holdout test set. The model was evaluated using area under the receiver operating characteristic curve (AUC) and sensitivity. Saliency maps were used for model interpretability to highlight relevant pixels for model decisions.

Results: The cross-validation AUC was 0.995 ± 0.010. The testing AUC was 0.909 and class-wise sensitivities were 0.88 (low risk) and 0.79 (high risk). The density plot (Figure, *B*) shows that the classifier correctly identifies both classes with confidence. Model interpretability using saliency maps (Figure, *C*) shows pixels corresponding to carotid artery vessel edges and in high-risk cases, carotid plaques.

Conclusions: Using this proof-of-concept model, carotid US long axis images are sufficient to identify high-risk plaques in symptomatic patients; we now need to determine whether we can identify high-risk plaques before symptoms to prevent devastating stroke caused by carotid disease.

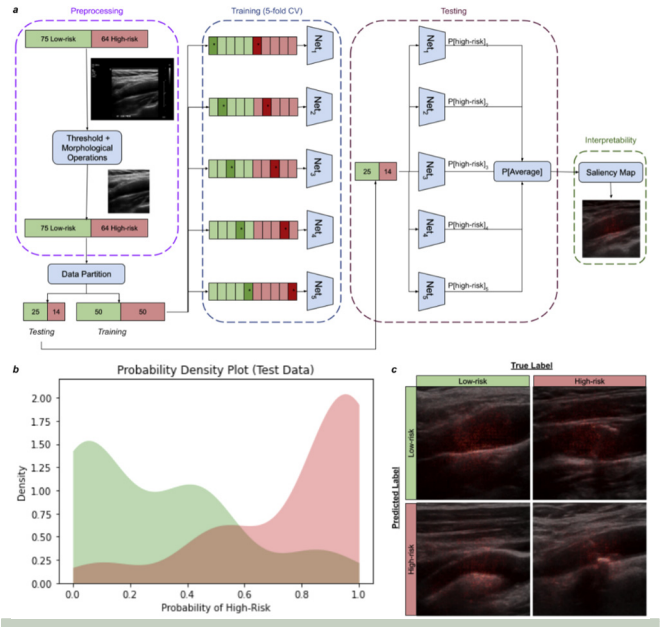

Fig.

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Transforming Growth Factor-beta Signaling Mediates Endothelial-to-mesenchymal Transition during Arteriovenous Fistula Remodeling in the Chronic Kidney Disease Environment

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Objectives: Arteriovenous fistulae (AVF) are the optimal conduit for hemodialysis access in patients with end-stage chronic kidney disease (CKD); however, AVF have high rates of failure due to aggressive neointimal hyperplasia. Neointimal hyperplasia in the CKD environment is characterized by endothelial-to-mesenchymal transition. We hypothesized that endothelial transforming growth factor (TGF)-β signaling promotes endothelial-to-mesenchymal transition to cause AVF failure.

Methods: Aortocaval AVF were created in C57BL/6J mice, with control mice having sham procedures. Three weeks before AVF, CKD was created via 5/6 nephrectomy (Nx); five groups were tested, including sham, sham+5/6Nx, AVF+0/6Nx, AVF+3/6Nx, and AVF+5/6Nx. Endothelial cell (EC)-and smooth muscle cell (SMC)-specific TGFβRI II knockout (KO) mice were treated with tamoxifen 2 weeks before AVF; ultrasound examination was used to determine AVF diameter and patency at postoperative days 7, 14, and 21. AVF were harvested at days 7 or 21 and examined with histology, Immunofluorescence and Western blot.

Results: There was no difference between mice treated with 0/6Nx or 3/6Nx regarding AVF diameter, AVF wall thickness, or accumulation of extracellular matrix components fibronectin, collagen 1, and collagen 3; however, AVF diameter was significantly decreased in mice treated with 5/6Nx compared with 0/6Nx or 3/6Nx, whereas there was increased AVF wall thickness as well as immunoreactivity of fibronectin ($P = .031$), collagen 1 ($P = .022$), collagen 3 ($P = .005$), and TGF-β1 ($P = .022$), compared with 0/6Nx. ECs in the AVF of mice treated with 5/6Nx had significantly increased immunoreactivity of the mesenchymal markers notch3 ($P < .0001$), vimentin ($P < .0001$), and FSP-1 ($P = .02$) compared with 0/6Nx. However, blocking TGFβ signaling using either EC-KO or SMC-KO mice had significantly decreased immunoreactivity of mesenchymal markers and wall thickness ($P < .0001$), consistent with reduced endothelial-to-mesenchymal transition and an increased diameter ($P = .035$). Interestingly, the AVF wall thickness in EC-KO mice was thinner than in SMC-KO mice.

Conclusions: Both EC- and SMC-specific TGF-β signaling promote endothelial-to-mesenchymal transition and wall thickening during venous remodeling in the CKD environment. These data suggest that the TGF-β signaling pathway may be a potential therapeutic target to prevent AVF failure.

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Altered Macrophage Response Associated with Impaired Skeletal Muscle Regeneration in a Murine Model of Limb Ischemia

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Introduction: Skeletal muscle regeneration in the ischemic limb is a complex process dependent on coordinated intercellular