KI REPORTS
KIReports.org

Association of Pathological Fibrosis With Renal Survival Using Deep Neural Networks

Vijaya B. Kolachalama[1,2,3,8], Priyamvada Singh[4,8], Christopher Q. Lin[5], Dan Mun[6], Mostafa E. Belghasem[7], Joel M. Henderson[7], Jean M. Francis[4], David J. Salant[4] and Vipul C. Chitalia[2,4]

[1]Section of Computational Biomedicine, Department of Medicine, Boston University School of Medicine, Boston, Massachusetts, USA; [2]Whitaker Cardiovascular Institute, Boston University School of Medicine, Boston, Massachusetts, USA; [3]Hariri Institute for Computing and Computational Science & Engineering, Boston University, Boston, MA, USA; [4]Renal Section, Department of Medicine, Boston University School of Medicine, Boston, Massachusetts, USA; [5]College of Engineering, Boston University, Boston, Massachusetts, USA; [6]College of Health & Rehabilitation Sciences: Sargent College, Boston University, Boston, Massachusetts, USA; and [7]Department of Pathology and Laboratory Medicine, Boston University School of Medicine, Boston, Massachusetts, USA

Introduction: Chronic kidney damage is routinely assessed semiquantitatively by scoring the amount of fibrosis and tubular atrophy in a renal biopsy sample. Although image digitization and morphometric techniques can better quantify the extent of histologic damage, we need more widely applicable ways to stratify kidney disease severity.

Methods: We leveraged a deep learning architecture to better associate patient-specific histologic images with clinical phenotypes (training classes) including chronic kidney disease (CKD) stage, serum creatinine, and nephrotic-range proteinuria at the time of biopsy, and 1-, 3-, and 5-year renal survival. Trichrome-stained images processed from renal biopsy samples were collected on 171 patients treated at the Boston Medical Center from 2009 to 2012. Six convolutional neural network (CNN) models were trained using these images as inputs and the training classes as outputs, respectively. For comparison, we also trained separate classifiers using the pathologist-estimated fibrosis score (PEFS) as input and the training classes as outputs, respectively.

Results: CNN models outperformed PEFS across the classification tasks. Specifically, the CNN model predicted the CKD stage more accurately than the PEFS model ($\kappa = 0.519$ vs. 0.051). For creatinine models, the area under curve (AUC) was 0.912 (CNN) versus 0.840 (PEFS). For proteinuria models, AUC was 0.867 (CNN) versus 0.702 (PEFS). AUC values for the CNN models for 1-, 3-, and 5-year renal survival were 0.878, 0.875, and 0.904, respectively, whereas the AUC values for PEFS model were 0.811, 0.800, and 0.786, respectively.

Conclusion: The study demonstrates a proof of principle that deep learning can be applied to routine renal biopsy images.

Kidney Int Rep (2018) ■, ■–■; https://doi.org/10.1016/j.ekir.2017.11.002
KEYWORDS: histology; machine learning; renal fibrosis; renal survival
© 2017 International Society of Nephrology. Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

From self-driving cars to face recognition, artificial intelligence and machine learning (ML) algorithms are being widely applied to enhance human endeavors. Over the last few years, the scientific community has witnessed a rapid increase in the adoption of cutting-edge data analytic tools such as ML to address several questions in clinical medicine.[1–6] ML techniques give computers the ability to integrate discrete sets of data in an agnostic manner to find hidden insights and to generate a disease-specific fingerprint. These tools are now being rapidly adopted in several specialties as unbiased, self-learning approaches for pathologic assessment. Such a framework can leverage hundreds to thousands of images as inputs and allow for objective quantification, followed by their association with several clinical outcomes of interest. ML techniques also have the potential to uncover several nonintuitive features that may be clinically relevant and hypothesis generating, as demonstrated in other disease scenarios.[7]

Although the trained eyes of expert pathologists are able to gauge the severity of disease and to detect

Correspondence: Vijaya B. Kolachalama, Boston University School of Medicine, 72 East Concord Street, Evans 636, Boston, Massachusetts 02118, USA. E-mail: vkola@bu.edu

[8]The first 2 authors contributed equally to this work.

Received 7 August 2017; revised 4 October 2017; accepted 6 November 2017

nuances of histopathology with remarkable accuracy, such expertise is not available in all locations, especially at a global level. Moreover, there is an urgent need to standardize the quantification of pathological disease severity, such that the efficacy of therapies established in clinical trials can be applied to treat patients with equally severe disease in routine practice. The tools to do this are at hand in the form of digitized images of pathology sections prepared with routine stains and ML algorithms. Such methods have already been tested and shown to be reliable for the analysis of malignancies such as cancer.[7–17] The application of deep learning frameworks, such as convolutional neural networks (CNN) for object recognition tasks, is proving to be especially valuable for classification of several diseases.[8–29]

To test the feasibility of applying ML technology to the analysis of routinely obtained kidney biopsy samples, we performed a proof-of-principle study on kidney biopsy sample sections with various amounts of interstitial fibrosis as revealed with Masson trichrome stain (Figure 1). Using an established CNN that relies on pixel density of digitized images,[30] we analyzed the ability of the ML technique to quantify the severity of disease as determined by several clinical laboratory measures and renal survival (Supplementary Figure S1). CNN model performance was then compared with that of the models generated, using the amount of fibrosis reported by an expert nephropathologist as the sole input and corresponding laboratory measures and renal survival as the outputs.

METHODS

Data Collection

A retrospective analysis of renal biopsy findings was performed on patients treated at the Boston Medical Center (BMC) between January 2009 and December 2012. Reports from all follow-up visits between 2009 and 2016 for these patients were also reviewed. All patient data were collected under protocol H-32289, which was reviewed and approved by the Institutional Review Board at Boston University Medical Campus. More than 300 biopsy samples were processed at BMC, of which 171 biopsy slides were available for subsequent imaging. These biopsy samples were obtained from adult patients who had 1 or more native or renal allograft biopsies, independent of the indication for the biopsy procedure. The only criterion for inclusion was the availability of pathological slides and accompanying clinical data. Several demographic and clinical features (including estimated glomerular filtration rate [eGFR], baseline creatinine, nephrotic-range proteinuria, etc.) were collected on these patients at the time of biopsy (Table 1). The 4-parameter Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula was used to calculate eGFR. A detailed chart review of the patients' electronic medical record was used to estimate 1-, 3-, and 5-year renal survival (see Supplementary Material for details of clinical data collection). Renal survival was measured as the time from the day of biopsy until the patient had 1 of the following events: initiation of dialysis, renal transplant, or all-cause mortality.

Imaging

Kidney biopsy samples were obtained in the form of individual trichrome-stained slides. Each selected core was imaged at ×40, ×100, and ×200 magnifications using a Nikon Eclipse TE2000 microscope (Melville, NY; http://www.bumc.bu.edu/busm/research/cores/). For ×40

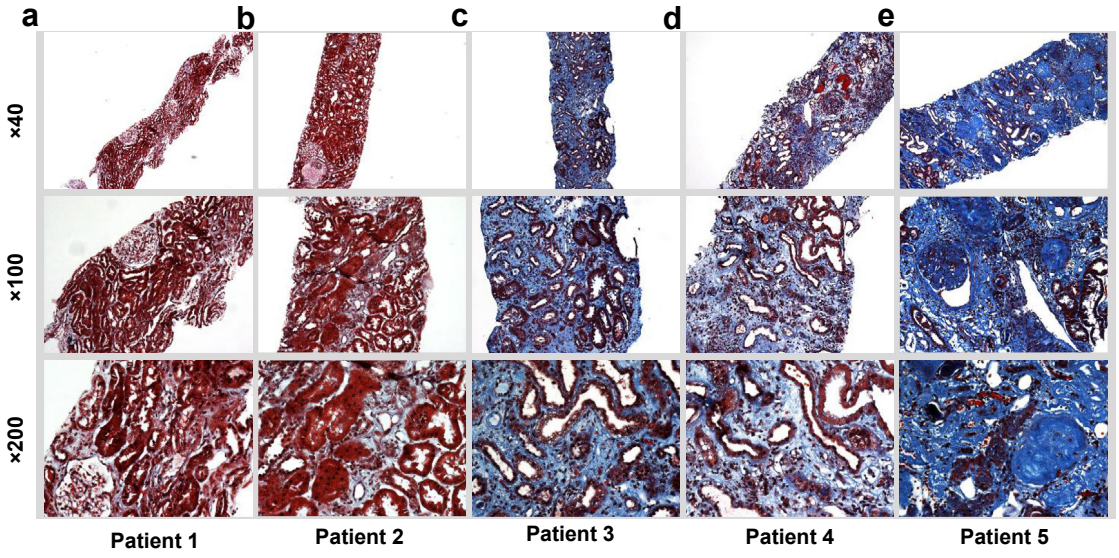

Figure 1. Sample interstitial fibrosis cases from the patient cohort. The trichrome-stained images demonstrate the variability and extent of interstitial fibrosis observed within renal biopsy samples at different magnifications. The in-house nephropathologist–derived fibrosis score was 5% to 10% for (a), 20% for (b), 30% for (c), 50% for (d), and 85% for (e).

Download English Version:

https://daneshyari.com/en/article/8773810

Download Persian Version:

https://daneshyari.com/article/8773810

Daneshyari.com