Progression of Diabetic Retinopathy in the Hypertension Intervention Nurse Telemedicine Study

Interventions to improve glycemic control reduce the progression of diabetic retinopathy. Additionally, pharmacologic reduction of blood pressure (BP) in patients with diabetes mellitus and poorly controlled hypertension reduces the risk of worsening diabetic retinopathy. Despite pharmacologic improvements, hypertension remains poorly controlled in approximately half of Americans with it. The Hypertension Intervention Nurse Telemedicine Study (HINTS) investigated a telemedicine-mediated medication management and behavioral intervention for hypertension. Participants in HINTS (including nondiabetic individuals) with poor BP control who received combined medication and behavioral management demonstrated mean decreases in systolic BP of 15 mm Hg and 8 mm Hg at 12 and 18 months, respectively. The purpose of the current analysis was to determine whether the interventions influenced the progression of diabetic retinopathy in participants with diabetes.

Methods | Eligibility criteria for HINTS included veterans having hypertension with inadequate BP control (average BP in past 12 months >140/80 mm Hg). Patients were excluded for hemodialysis or a creatinine level greater than 2.5 mg/dL (to convert to micromoles per liter, multiply by 88.4). All participants received home BP monitors. Participants were randomized to the following: (1) usual care; (2) nurse-administered behavioral intervention; (3) nurse-administered medication management; or (4) a combination of the 2 interventions (Table). In institutional review board–approved secondary analyses of diabetic participants, a single chart abstractor (K.W.M.) determined the presence and severity of diabetic retinopathy at baseline and the most recent follow-up, as recorded by the eye care provider of record in the electronic chart. Eligible participants had at least 1 documented dilated examination prior to or within 2 months of enrollment and at least 1 subsequent dilated examination 365 days or later following enrollment. Progression was defined as one or both eyes moving 1 or more steps along the spectrum of retinopathy: none, mild nonproliferative, moderate nonproliferative, severe nonproliferative, proliferative, and visual acuity less than 20/60 in the better-seeing eye. Logistic regression was used to examine the association between progression of diabetic retinopathy and the intervention group, adjusting for baseline hypertension control and duration of follow-up.

Results | Of the 593 veterans enrolled in HINTS, 252 were identified as diabetic. Of the 194 participants meeting the additional criteria for documented eye examinations, 58 (30%) had diabetic retinopathy at baseline and 65 (34%) experienced progression of retinopathy in at least 1 eye at follow-up (mean [SD] follow-up, 1255 [344] days; median follow-up, 1310 days). After controlling for duration of follow-up, the odds of diabetic retinopathy progression were significantly greater among participants receiving usual care than among participants receiving medication management, either alone or in combination with behavioral management (odds ratio = 2.16; 95% CI, 1.03-4.52; P = .04), but not different from the group receiving behavioral management alone (odds ratio = 0.88; 95% CI, 0.40-1.95; P = .84).

Discussion | A nurse-administered medication management program facilitated by home BP monitoring was associated with decreased risk of progression of retinopathy in diabetic individuals with comorbid hypertension. Although intensive pharmacologic control of systolic BP (<120 mm Hg) may not be pro-

![Figure. Intraocular Pressure Before, During, and After Glucosamine Supplementation](attachment:figure.png)
Letters

In early disease.6 Although as a secondary analysis of this study are consistent with other work suggesting that BP control is most helpful in controlling diabetic retinopathy of this study, likely limiting the population to diabetic individuals with less severe retinopathy. As such, the results of this study are consistent with other work suggesting that BP control is most helpful in controlling diabetic retinopathy in early disease.6 Although as a secondary analysis this study is limited in the ability to support causation (for example, less progression of retinopathy in the combined intervention group may be related to the intervention but not a direct result of decreasing BP), the potential benefit of telemedicine interventions targeting BP control in patients at risk for diabetic eye disease is encouraging and warrants further study.

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Long-term Suppression of Multidrug-Resistant Cytomegalovirus Retinitis With Systemically Administered Leflunomide

Cytomegalovirus (CMV) infection continues to affect outcomes in transplant recipients. Typical CMV antivirals, including ganciclovir sodium and its oral prodrug valganciclovir hydrochloride, foscarnet sodium, and cidovir, are DNA polymerase inhibitors. Resistance of CMV to this class of drugs is an ongoing challenge. Alternative CMV antivirals include leflunomide and cytomegalovirus immunoglobulin.1-3

We report the follow-up of a renal transplant recipient who developed bilateral ganciclovir-resistant CMV retinitis that has been treated with leflunomide since July 2004.4

Report of a Case | In March 2002, a 43-year-old CMV IgG-negative woman underwent cadaveric renal transplantation from a CMV IgG-positive donor. Despite ganciclovir prophylaxis, she developed CMV viremia with retinitis. She was placed on treatment doses of ganciclovir and was stable for 14 months. At month 18 following transplantation, she developed bilateral uveitis and reactivation CMV retinitis.

She was referred to the infectious diseases clinic at the University of Colorado and was initially treated with intravenous ganciclovir and CMV immunoglobulin. Intravenous foscarnet, oral valganciclovir, and weekly CMV immunoglobulin were initiated, with remission of the retinitis. Subsequent reactivation retinitis was treated with ganciclovir implantation4 without response. Weekly bilateral intraocular foscarnet injections were successful in the right eye only. Genotyping of the

Table. Characteristics of Subjectsa

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<thead>
<tr>
<th>Characteristic</th>
<th>Randomization Group</th>
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<tbody>
<tr>
<td></td>
<td>Usual Care (n = 49)</td>
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<tr>
<td>Sex, No.</td>
<td></td>
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<tr>
<td>Male</td>
<td>48</td>
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<tr>
<td>Female</td>
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<tr>
<td>Race, No.</td>
<td></td>
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<tr>
<td>White</td>
<td>23</td>
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<tr>
<td>Nonwhiteb</td>
<td>26</td>
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<tr>
<td>Follow-up, mean (SD), d</td>
<td>1265 (385)</td>
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<tr>
<td>Diabetic retinopathy in either eye, No. (%)</td>
<td></td>
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<tr>
<td>Presence at baselinea</td>
<td>15 (31)</td>
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<tr>
<td>Progression, No. (%)c</td>
<td>20 (41)</td>
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</tbody>
</table>

a Diabetes was defined as self-reported history of diabetes or diagnosis of diabetes listed in the medical record.

b Two subjects in the nonwhite category self-identified as American Indian and the remainder identified as African American.

Defined as documented before or within 2 months of study enrollment.

c Defined as progression from absence to presence or less severe to more severe from the time of enrollment to the most recent follow-up 365 days or later following enrollment.