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Diabetic Retinopathy: Where We Were, Where We Are, and Where We Need to Go

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Diabetic retinopathy continues to be a significant cause of vision loss. However, we currently have more treatment options than ever before, such as vascular endothelial growth factor inhibitors, to offer our patients. This issue of *Ophthalmology Rounds* summarizes our current understanding of diabetic retinopathy, current treatment modalities, and offers suggestions for improving the care of our patients in the future.

Diabetes is a Canadian epidemic. In 2010, the Canadian Diabetes Association (CDA) estimated that 2. 7 million Canadians were living with diabetes, and approximately 1 million more were believed to be unaware they had the disease.[1] The CDA projects that up to 4.2 million Canadians will have diabetes by 2020.

According to the Public Health Agency of Canada,[2] 35% of Canadians with diabetes reported having eye problems, such as diabetic retinopathy, cataracts, and glaucoma; this percentage was significantly more than that for any other diabetes-related complication. Approximately 482 000 Canadians had some form of diabetic retinopathy in 2006, 103 000 of which was a vision-threatening form.[3] By 2031, these numbers are expected to increase to 777 000 and 158 000, respectively. The recent Canadian Ophthalmological Society (COS) diabetic retinopathy guidelines estimate, based on findings by Fong et al,[4] that almost all patients with type 1 diabetes and more than 60% of those with type 2 diabetes will have some degree of retinopathy within 20 years of diagnosis of their diabetes.[5]

Estimates of the prevalence and rates of progression of diabetic retinopathy among people with diabetes vary and are dynamic due to technological improvements in diabetes care, such as the widespread availability of continuous insulin infusion pumps. For example, the Wisconsin Epidemiologic Study of Diabetic Retinopathy (WESDR)[6] evaluated a cohort of type 1 diabetes patients receiving primary care in Wisconsin from 1979-1980.The 25-year cumulative rate of progression of diabetic retinopathy was 83%: however, this number would likely be lower in the same cohort diagnosed today given advances in medical management. Progression was positively correlated to factors such as male sex and elevations in glycosylated hemoglobin and diastolic blood pressure (BP).

Systemic Medical Therapy

Despite the fact that the specific ophthalmoscopic features of diabetic retinopathy have been known since the 19th century, effective therapies began to emerge only in the 1960s. In fact, at one time proliferative diabetic retinopathy was treated with pituitary ablation.[7] Although systemic medical intervention for the prevention of diabetic retinopathy usually falls under the realm of the primary care provider or endocrinologist, it is important for ophthalmologists to be aware of the medical interventions available and, as a member of the patient's healthcare team, to stress adherence to the overall medical plan and whole-body health.

A cross-sectional study from England found that a significant percentage of patients with diabetes seen in the eye clinic with diabetic retinopathy are not optimally medically

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managed, and concluded that we as ophthalmologists can play a larger role in encouraging primary prevention in our patients.[8] Important risk factors that are managed medically include hyperglycemia, hypertension, and dyslipidemia.[5]

Blood glucose

The landmark multicentre, randomized, controlled Diabetes Complications and Control Trial (DCCT),[9,10] the United Kingdom Prospective Diabetes Study (UKPDS),[11] and the more recent Action to Control Cardiovascular Risk in Diabetes (ACCORD) study[12] conclusively demonstrated that tight glycemic control through intensive insulin therapy significantly reduced the risk of developing retinopathy and slowed progression of existing retinopathy. Of note, "intensive control" in the DCCT consisted of just 3 insulin injections per day or insulin pump therapy, which would be considered standard therapy in the newer studies and symbolizes the advances in standard of care over time.[9,10,12]

Despite being the strongest risk factor, however, glycated hemoglobin accounted for only 11% of the risk of retinopathy in the DCCT and, combined with BP and serum cholesterol, only 9%–10% of the risk of retinopathy in the WESDR.[6] This finding suggests that other modifiable risk factors are important in disease prevention. The average glycated hemoglobin values from the DCCT were 7.2% in the intensive therapy group and 9.1% in the conventional group over an average of 6.5 years of follow-up.[9,10] In contrast, intensive glucose control in the ACCORD[12] study was defined as glycated hemoglobin <6%. However, the intensive-control arm of the ACCORD study was stopped early due to increased rates of severe hypoglycemic events requiring medical intervention and increased rate of death from any cause, suggesting that there is a threshold where the benefits of tight glycemic control on microvascular complications are outweighed by deleterious effects of hypoglycemia. This threshold is likely different for every patient, and individualized treatment is warranted to appropriately balance tight glucose control with safety.

Blood pressure (BP)

Antihypertensive therapy is used widely in patients with diabetes to prevent macrovascular complications. As stated previously, the WESDR[6] found that elevated diastolic BP is an important risk factor for diabetic retinopathy. Likewise, results of the UKPDS showed that tight blood pressure control (<150/85 mm Hg) reduced the clinical complications of diabetic retinopathy,[13] and the Meta-Analysis for Eye Disease (META-EYE) Study Group[14] (35 studies) concluded that the prevalence of retinopathy was higher with a BP >140/90 mm Hg. In contrast, intensive BP therapy in the ACCORD trial[12] was associated with a slightly higher rate of progression of diabetic retinopathy over the 4-year study period.

Cholesterol

Modification of risk of diabetic retinopathy with treatments for dyslipidemia is currently an avenue of research of great interest. The Fenofibrate Intervention and Event Lowering in Diabetes (FIELD) study[15] found that, while fenofibrate therapy did not significantly affect the primary cardiovascular outcomes, it significantly reduced the need for laser photocoagulation compared with placebo. Similarly, the ACCORD trial[12,16] showed that combination therapy with fenofibrate plus simvastatin reduced the odds progression to diabetic retinopathy by 40% (6.5% versus 10.4%; P=0.006). Interestingly, fenofibrates seem to exert their benefits through mechanisms that are independent of serum lipid lowering.[15-17]

Laser Therapy

Until recently, laser photocoagulation was the gold standard of treatment for proliferative diabetic retinopathy and diabetic macular edema (DME), as supported by the Diabetic Retinopathy Study and Early Treatment of Diabetic Retinopathy Study (ETDRS) programs. More than 35 years ago, the Diabetic Retinopathy Study[18] concluded that panretinal photocoagulation (PRP) for high-risk proliferative diabetic retinopathy decreased the risk of severe vision loss by greater than 50%. Since then, ophthalmologists have used PRP to prevent severe vision loss in patients with diabetic retinopathy. The ETDRS[19] introduced the term "clinically significant macular edema" (CSME), and created the ETDRS visual acuity (VA) chart, which is almost universally used in the newer research studies. This study provided our basis for treating CSME with macular focal or grid laser. Laser therapy can be very effective and remains first-line treatment for proliferative diabetic retinopathy and specific cases of DME. The COS guidelines recommend focal laser as first-line therapy for CSME without central macular thickening.[5] Results of widely published laser studies are well known to ophthalmologists and are beyond the scope of this article.

Vascular Endothelial Growth Factor (VEGF) Inhibitors

The use of intravitreal anti-VEGF therapy is revolutionizing the treatment of DME and may also have a role to play in the treatment or prevention of proliferative diabetic retinopathy.[20] The COS recommends VEGF inhibitors, alone or combined with focal laser,

Table 1: Primary outcomes of VEGF studies

READ-2[20-22]			
Mean change in BCVA (letters)	6 months (N=126)	24 months (N=101)	36 months (N=74)
Ranibizumab	+7.2	+7.7	+10.3
Laser	-0.4	+5.1	+1.4
Ranibizumab + laser	+3.8	+6.8	+8.9
RISE/RIDE[23,24]			
Percent gain of ≥15 letters	RISE – 2 year (N=377)	RIDE – 2 year (N=382)	Pooled – 3 year (N=759)
Ranibizumab 0.3 mg	44.8%	33.6%	44.0%
Ranibizumab 0.5 mg	39.2%	45.7%	40.9%
Sham injection[a]	18.1%	12.3%	20.6%
Mean change in BCVA (letters)			
Ranibizumab 0.3 mg	+12.5	+10.9	+12.4
Ranibizumab 0.5 mg	+11.9	+12.0	+11.2
Sham injection[a]	+2.6	+2.3	+4.5
DRCRnet[25-27]			
Mean change in VA (letters)	1 year (N=854 eyes)	2 years (N=628 eyes)	3 years (N=291 eyes)
Ranibizumab + prompt laser	+9	+7	+6.8
Ranibizumab + deferred laser	+9	+9	+9.7
Triamcinolone + prompt laser	+4	+2	–
Sham injection + prompt laser	+3	+3	–
RESOLVE[28]			
Mean change in BCVA (letters) from baseline to month 1–12			1 year (N=151)
Ranibizumab (pooled 0.3 mg and 0.5 mg results)			+7.8
Sham injection			-0.1
RESTORE[29,30]			
Mean change in BCVA (letters) from baseline to month 1–12		1 year (N=345)	2 years (N=220)
Ranibizumab + sham laser		+6.1	+7.9
Ranibizumab + laser		+5.9	+6.7
Sham injection + laser		+0.8	–
BOLT[31,32]			
Mean change in BCVA (letters)		1 year (N=80)	2 years (N=80)
Bevacizumab		+5.6	+8.6
Laser		-4.6	-0.5

Mean changes are from baseline levels. [a]Control patients in the RISE/RIDE extension received ranibizumab 0.5 mg

VEGF = vascular endothelial growth factor; BCVA = best-corrected visual acuity

for CSME with central macular thickening.[5] Currently, ranibizumab, an affinity maturated monoclonal antibody fragment (Fab) to VEGF-A, and bevacizumab, a humanized monoclonal antibody to VEGF-A, are commonly used in Canada; however, bevacizumab has not been approved by Health Canada for intraocular use, and its use is considered to be "off-label".

A number of important clinical trials support the use of VEGF inhibitors for the treatment of DME (Table 1). Results of the READ-2 trial[20-22] (N=126) indicated that intraocular 0.5-mg injections of ranibizumab were superior to laser photocoagulation (focal or grid) in increasing best-corrected VA (BCVA; primary outcome); however, improvements in anatomical parameters were greater with laser treatment and highest with combined laser and ranibizumab. Ranibizumab was injected at baseline, 1, 3, and 5 months, laser photocoagulation was

performed at baseline and (if necessary) at 3 months, and combination therapy was administered at baseline and at 3 months. After 6 months, patients were evaluated every 2 months and re-treated as necessary. Mean changes in BCVA at 6 months were +7.2 letters with ranibizumab, -0.4 letters with laser, and +3.8 with combination therapy. After 2 years, the mean improvements in BCVA were 7.7, 5.1, and 6.8 letters, respectively. It should be noted that after the primary endpoint at 6 months, patients in the laser group could receive injections of ranibizumab if their subfield thickness >250 µm, and one could postulate that the improvement in 2-year BCVA may be due to these injections. Measurement of subfield thickness revealed a significant reduction with ranibizumab at 6 months, but increases at 12 and 24 months despite further injections, whereas the laser and combined groups experienced steady declines in subfield thickness up to month 24. Since there was no significant difference in BCVA at year 2, the READ-2 researchers suggested that combined laser and ranibizumab is beneficial since this treatment strategy achieved a better anatomic outcome with fewer injections overall. In the third year of the study, patients were seen monthly and if met the re-treatment criteria were given intravitreal ranibizumab. Of note, 50% of the ranibizumab group met re-treatment criteria more than 6 times in the third year compared to 8% of the ranibizumab plus laser and 18% of the laser group suggesting that patients need to be followed more closely and may require more frequent injections long term. That being said, the ranibizumab only group did obtain the greatest benefit regarding visual acuity.[22] Also of interest was the significantly heterogeneic response of patients in each group, suggesting that the ideal treatment regiment is highly patient specific.

The multicentre, double-masked, sham-injection controlled, randomized RISE and RIDE trials[23,24] (N=377 and 382, respectively) supported the effectiveness of ranibizumab in the management of DME over 2 years. Patients received either ranibizumab (0.3 mg or 0.5 mg) or monthly sham injections, and were eligible for rescue laser after month 3. Gains of ≥15 letters (primary outcome) were observed in 44.8% and 39.2% with ranibizumab 0.3 mg/month and 0.5 mg/month, respectively, compared with 18.1% of controls in RISE. The respective 24-month outcomes in RIDE were 33.6% (0.3 mg/month), 45.7% (0.5 mg/month), and 12.3% (sham). Improvements were seen as early as 7 days after injection. As expected, more sham-treated patients required macular laser or PRP for proliferative diabetic retinopathy (mean 1.8 and 1.6 procedures) over 24 months compared with patients receiving ranibizumab (0.3–0.8 procedures), and fewer ranibizumab patients experienced significant vision loss compared to sham controls. Anatomic outcome was also superior in the ranibizumab treated groups and ranibizumab patients were less likely to develop proliferative diabetic retinopathy. Safety outcomes were consistent with other trials of ranibizumab. Deaths of vascular or unknown cause and cerebrovascular accidents were slightly more common in patients treated with ranibizumab (combined incidence 2.4% in the ranibizumab groups versus 1.2% for controls). The extension to 3 years, in which all patients received ranibizumab, revealed that VA gains were preserved in subjects who had received the agent previously in the study (+11.2–12.4 letters); gains were also seen in patients previously randomized to sham injection, but not as extensive as those originally in ranibizumab groups.[24]

The Diabetic Retinopathy Clinical Research Network (DRCRnet)[25-27] compared the use of ranibizumab (0.5 mg) plus prompt or deferred laser to triamcinolone (4 mg) plus prompt laser to laser alone with sham injections for centre-involving DME. A total of 854 eyes in 691 participants were studied. Patients in the ranibizumab group were treated with monthly injections until month 3, after which injections were at the investigators' discretion, based on a complicated retreatment algorithm. Triamcinolone could be injected every 16 weeks as needed, with sham injections in between. At the initial 1-year endpoint,[24] investigators found that ranibizumab with prompt or deferred laser was significantly more effective in improving VA letter scores (+9±11 [P<0.001] with prompt laser and +9±12 [P<0.001] with deferred laser) than laser alone (+3±13); triamcinolone with laser was slightly more effective (+4±13; *P*=0.31). Of note, in pseudophakic eyes, VA improvements in the triamcinolone group were similar to those observed with ranibizumab; however, there was a modest increase in intraocular pressure (IOP) with triamcinolone. After 2 years,[25] the mean letter gains in the ranibizumab plus prompt laser and the ranibizumab plus deferred laser groups were +4 and +6, respectively, more than the laser-only group. Those receiving triamcinolone plus prompt laser fared worse (-1 letters) than laser alone, which was likely secondary to cataract formation. Pseudophakic eyes in the triamcinolone group gained a mean of 1.6 letters more than the laser group, which was more than that observed with ranibizumab plus prompt laser (+0.5) but less than ranibizumab plus deferred laser (+3.5 letters). Three-year follow-up[27] showed that the deferred laser group achieved 2.9 more letters in visual acuity compared to the prompt laser group (*P*=0.02). More than half (54%) of the deferred

laser group never required laser and the median number of injections required over 3 years was 12 in the prompt laser group and 15 in the deferred group.

The 12-month, multicentre, double-masked RESOLVE study[28] (N=151) compared monthly ranibizumab (0.5 mg and 0.3 mg) to sham injection (pressing of the blunt tip of a syringe to an anesthetized eye). Injections were monthly until the third month after which injections were based on a study specific re-treatment algorithm. Dose doubling was allowed, and occurred in 68.6% of subjects further to a central retinal thickness of >300 µm or a <50-µm reduction in retinal edema after 1 month, as per protocol design. The overall average change in BCVA from baseline to months 1-12 (primary endpoint) was +7.8 letters in the ranibizumab groups compared to -0.1 letters in the sham group ($P<0.0001$). Two patients developed endophthalmitis and 1 patient had a myocardial infarction (MI), thought to be related to anti-VEGF treatment. Interestingly, 3 patients developed antibodies to ranibizumab after treatment.

In the 12-month, multicentre, double-masked RESTORE study[29] (N=345), ranibizumab alone (sham laser) or combined with macular laser were compared with laser monotherapy (sham injection) in the treatment of DME. Results were consistent with previous studies: the patients treated with ranibizumab alone and with laser experienced superior outcomes compared to laser alone in terms of mean improvements in BCVA (+6.1 and +5.9 versus +0.8, respectively; both $P<0.0001$). A greater proportion of ranibizumab-treated patients gained >15 letters, central retinal thickness was reduced significantly more with ranibizumab, and quality of life was significantly improved with ranibizumab compared with laser only as measured by the National Eye Institute Visual Function Questionnaire. No endophthalmitis occurred in the study. Though not statistically significant, 6 arterial thromboembolic events occurred in the ranibizumab alone group compared to 1 in the ranibizumab plus laser and 1 in the laser alone group. Since laser is unlikely to be protective against these events, the study authors stated that ranibizumab was not associated with an increased risk of arterial thromboembolic events since the ranibizumab plus laser group had the same number of events as laser alone. Nevertheless, readers should take note of these events in the ranibizumab-alone group within the wider discussion of the systemic safety of ocular anti-VEGF therapy. The RESTORE open-label extension study[30] (N=240) is treating 240 of the original RESTORE study population with ranibizumab 0.5 mg; patients are also eligible to receive laser according to the ETDRS guidelines. At 1 year of follow-up in the extension, gains in mean BCVA were preserved with ranibizumab, and adverse events were consistent with the published safety profile. Four deaths were reported, none of which were believed to be related to the study treatments. The investigators found that an average of 3.8 injections were enough to preserve these visual gains over the first year of the extension phase.

The 2-year single-centre, randomized, controlled Bevacizumab Or Laser Therapy (BOLT) trial[31,32] compared intravitreal bevacizumab with macular laser therapy in the treatment of subjects (N=80) with centre-involving CSME. Those in the bevacizumab arm received intraocular injections at baseline, and 6 and 12 weeks; additional injections were given on an as-needed basis. Subjects in the laser-treated group were retreated if clinically indicated by EDTRS guidelines. At 1 and 2 years, the mean gains in BCVA were 5.6 and 8.6 letters, respectively, in the bevacizumab group and losses of 4.6 and 0.5 letters, respectively in the laser group ($P=0.0006$ [1 year] and 0.001 [2 years]). Bevacizumab reduced the mean central macular thickness more than laser (146 m versus 118 m, respectively). However, the injection group required a median number of 13 injections compared to only 4 laser treatments. There were no cases of endophthalmitis reported in the study. Two of the patients in the bevacizumab group experienced an MI while none had cerebrovascular accidents; in the

Table 2: Systemic processes in which VEGF is involved[33]

- Cell survival
  - Alveolar septal cells
  - Neural cells
  - Pancreatic islet cells
- Cardiac development
- Vasodilation and vascular permeability
- Neovascularization following myocardial infarction and stroke
- Endothelial cell proliferation, survival, and recruitment
- Lung maturation
- Dendritic cell differentiation and function
- Bone growth and fracture healing
- Female reproductive function
- Kidney function and glomerulogenesis
- Protection of hepatic cells from toxic damage,
- Enzyme induction
  - Plasminogen activator
  - Endothelial nitric oxide
  - Matrix metalloproteinases
- Maintenance of the microvasculature in many organs
- Monocyte/macrophage chemoattraction
- Regeneration of skeletal muscle
- Trophic support of choriocapillaris
- Wound healing

laser group, no MIs and 1 cerebrovascular accident were reported. Although beneficial results are seen with this study, the numbers are small and no conclusive evidence of ocular and systemic safety is known with bevacizumab. However, this study is important since many Canadian patients are treated with bevacizumab as opposed to ranibizumab due to lack of drug coverage and the large cost associated with ranibizumab (discussed later).

Two recent meta-analyses have evaluated trial data to date with ranibizumab and bevacizumab in the treatment of DME. In the ranibizumab meta-analysis (4 studies; N=1313), Wang et al[33] showed that the mean difference in BCVA statistically significantly favoured ranibizumab (P=0.0003) compared to non-drug controls, and favoured ranibizumab plus laser compared to laser alone (P=0.007 for 24-month data). Ranibizumab was likewise more effective in reducing CMT as monotherapy (P=0.02) and in combination with laser (P=0.01). Differences in adverse events between ranibizumab and non-ranibizumab treatment arms were not statistically significant. Goyal et al[34] (4 studies; N=484 eyes) showed that bevacizumab treatment reduced CMT statistically significantly greater than control at 6 weeks; however, this benefit lost its significance at 12–24 weeks. Similarly, BCVA improvement was statistically significant with bevacizumab at 6 weeks, but not at 12 weeks. Combination therapy with triamcinolone did not result in a significant increase in BCVA. The authors concluded that bevacizumab is effective in the short-term but its benefit wanes past 6 weeks.

We would argue that it is likely that a combination of anti-VEGF drugs with laser will prove to be the best treatment but will be very patient-specific.

Issues with VEGF Inhibitor Therapy

Cost

Cost of current anti-VEGF therapies is a barrier to treating all of our diabetic patients with these agents, whether patients pay out of pocket or whether the treatment is funded by the patient's respective provincial government. While laser treatment requires only the purchase and upkeep of the instrument and the time of the physician, the cost of ranibizumab can be in the thousands of dollars and bevacizumab in the hundreds of dollars per monthly injection per patient and require frequent examinations and diagnostic imaging.

Two recent cost-effectiveness analyses were conducted for VEGF inhibitors. The DRCRnet group[35] found that the incremental cost per letter gained with ranibizumab over 2 years compared to laser was $5943. In phakic patients with DME, ranibizumab plus deferred laser improved BCVA by 6 letters at an additional cost of $19 216 over 2 years compared to treating with triamcinolone; according to the authors, this would meet most cost-effectiveness standards provided these gains were maintained over subsequent years. However, they suggested that triamcinolone seems to be the most cost-effective treatment for DME in pseudophakic patients. Mitchell et al[36] examined the cost-effectiveness of ranibizumab versus laser therapy, applying a Markov model of simulated long-term outcomes and costs based on results of the RESTORE trial. They calculated a 0.17 gain in quality-adjusted life-years (QALYs) with ranibizumab at an incremental cost of £4191 ($6653 CDN) versus laser. The incremental cost-effectiveness ratio (ICER) was £24 028 ($38 139 CDN), with a 64% probability of being cost-effective at a threshold of £30 000 ($47 618 CDN) per QALY.

A cost:benefit discussion of this gain in BCVA should be initiated with each patient.

Safety

The safety of long-term intraocular anti-VEGF drugs has not been fully elucidated. None of the trials listed above have been powered to properly detect adverse events; cardiac trials have demonstrated that the number of patients needed to properly detect vascular events in a trial is in the range of ≥10 000.While the risk of endophthalmitis with a VEGF inhibitor is similar to that of any intraocular injection, there is a potential for systemic absorption by way of uveal vessels or the aqueous humour and subsequent systemic suppression of the VEGF cascade.[37] VEGF acts as a pleuripotent growth factor and is involved in numerous processes (Table 2).[38] Adverse events such as hypertension, proteinuria, hemorrhage, thromboembolic events, and gastrointestinal perforation are associated with intravenous bevacizumab used in chemotherapeutic regimens.[36]

A recent nested case-control study in Ontario by Campbell et al[39] involving 91 378 patients with retinal disease showed that intravitreal VEGF injections did not increase the risks of ischemic stroke, acute MI, venous thromboembolism, or congestive heart failure. Analysis of a diabetes subgroup showed a statistically significant association between acute MI and exclusive bevacizumab use when exclusive ranibizumab was used as the referent; however, this should be interpreted with caution as it may, as the authors suggest, be due to a type 1 error.

Until an eye study is appropriately powered to assess systemic adverse events of anti-VEGF treatment in patients with diabetes, these agents should be used with caution in patients at high risk of comorbidities and patients should be made aware of the risk.

Steroids

Intravitreal triamcinolone acetate (IVTA), a synthetic glucocorticoid, has also been used with some success to treat DME; however, sequelae such as cataract formation and raised IOP complicate this treatment. The DRCRnet group found that IVTA plus prompt focal/grid laser was superior to laser alone in VA outcome for pseudophakic patients with DME. This was comparable to treatment with ranibizumab in pseudophakic patients. It should be emphasized that this effect was only seen in the subset of pseudophakic patients.[26] A recent meta-analysis by Qi et al[40] found that IVTA was better than subtenon (ST) TA – advocated by some as a less invasive route of administration – at improving VA and decreasing central macular thickness at 1 and 3 months post-injection; however, this effect was lost in both treatment arms by 6 months. While both IVTA and STTA raised IOP at 1 and 3 months, only this pressure remained elevated at 6 months in the STTA group. IVTA is significantly less costly than anti-VEGF treatment and may be considered in pseudophakic patients with centre-involving DME.

Future Goals

Despite the significant progress in the treatment of diabetic retinopathy, people with diabetes are still going blind. Improvements in management and technology are all for naught if the patient never presents to us. Advances in screening and early detection need to keep pace with our interventions. Currently, though we have recommendations from the new COS guidelines on diabetic retinopathy,[5] there is no standardized diabetic retinopathy screening program across Canada. Furthermore, many diabetic patients live in remote communities and may never see an eye specialist. Also, it is questionable whether it makes sense to spend significant healthcare dollars treating diabetic eye disease with cutting-edge biologic therapies when our patients are not being sufficiently medically optimized. If the underlying problem is not properly addressed, the consequences will continue to occur. Even in large tertiary-care centres, there is little collaboration between primary-care providers, endocrinologists, cardiologists, nephrologists, neurologists, and ophthalmologists as we recently learned while conducting our own preliminary study. Until we have true multidisciplinary diabetes teams, it will be difficult to properly manage these complex, multisystem patients. We as ophthalmologists can and should be leaders in these teams with the goal of providing our diabetic patients with the best care possible, including the best odds of good vision and an excellent quality of life.

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