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Review

Diabetic retinopathy assessment: Towards an automated system

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ABSTRACT

The incidence of diabetes and diabetic retinopathy has been shown to be increasing worldwide. While ophthalmologists struggle to treat this retinopathy, they are also faced with an increment of diabetic referrals for eye screening. Screening and early detection of diabetic retinopathy are crucial to help reduce the incidence of visual morbidity and visual loss. In most countries, diabetic retinopathy assessments are done manually. This is time consuming and is a cause of additional clinical workloads. Clinicians are now aware of the need for an automated system for grading Diabetic Retinopathy (DR) that can help in tracing abnormalities in patients' retinas based on their fundus images, and assist in grading the retina conditions accordingly. This will lead to more effective assessment methods, as well as providing a second opinion to the ophthalmologist during diagnosis. This paper presents an overview of various methods of automated DR grading assessment systems that can complement manual assessments. Tortuosity of the blood vessels is introduced as one of the significant features that can be quantified and associated with DR stages for the grading assessment. From this review, it can be concluded that the automated system has a huge potential for wider acceptance in real life applications. However, there is still some space for improvement for a more robust system. Nevertheless, the DR automated grading assessment system is foreseen as being widely embraced by researchers and ophthalmologists in the future.

Contents

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1. Introduction

According to the World Health Organisation (WHO), in 2012 diabetes approximately caused 1.5 million deaths. From 2005 to 2008, 28.5% of diabetic patients above the age of 40 years were diagnosed with diabetic retinopathy (DR). Even worse, 4.4% of them developed advanced DR, which can lead to blindness [1]. The Singapore Malay Eye Study (SiMES) reported that one in ten Malay adults with diabetes in Singapore has vision threatening diabetic retinopathy [2]. In Malaysia, the 2007 Diabetic Eye Registry reported that the prevalence of DR was 36.8% among Malaysian adults and the National Eye Database (NED) reported that in 2008, 11.5% of patients had vision threatening DR [3]. Proper and early treatment of the diabetes disease is cost effective since the consequences of long term untreated diabetes are very expensive and may lead to severe DR progression [45,63]. There is a widespread consensus that an accurate diagnosis of DR followed by treatment can help prevent blindness and vision loss. Therefore, digital fundus images of the retina serve as an important screening platform for the ophthalmologist to diagnose and grade the severity of DR.

Researchers now seek to develop an automated detection system that can aid the ophthalmologist in this time consuming screening process. Abnormal DR features seen on a digital fundus image, such as microaneurysms that appear as small and round dark red dots, haemorrhages and exudates, are common features used to detect DR [4]. Haemorrhages can be seen when there are blood leaks around the infected retina. In addition, they also may appear as dot blots which may lead to white patches in the retina called cotton wool spots. The exudates occur when lipid leaks from the infected blood vessels in the retina [4]. The number of abnormalities in the area of the retina increase with the stage of the disease [5].

Other than these features, a few recent studies [6–8] have shown early evidence that retinal vascular tortuosity is associated with the development of DR and be the beginning of microvascular damage in diabetic patients [63]. The tortuosity of the vessels is difficult to quantify. Due to this fact, multiple measures have been applied to describe the tortuous vessel; for example a simple/normal curving and complex curving vessel [6–8,25–27,31,32,35,36,38–42,47,48,59–61]. However, the quantification methods employed to assess the retinal vascular tortuosity in these previous studies [6–8] are either subjective or inaccurately represent the tortuosity of the vessels in the DR disease growth [63]. Thus, it has become the motivation of this work to determine the association of retinal vessel tortuosity with DR severity stages. This paper focuses on the development of an automatic DR assessment system that integrates tortuosity as one of potential features to quantify and associate with DR stages (or severity scales). To the best of our knowledge, there is no comprehensive study and specific finding that demonstrate the association of tortuosity with DR severity stages [39].

This paper is divided into six sections. The introduction to Diabetic Retinopathy (DR) and extensive discussion of DR progression in diabetic patients from a (mild) nonproliferative stage to the severe stage, and then to the more advanced proliferative DR, are described in Section 2. DR medical assessments which consist of DR screening tools and grading are provided in Section 3. In Section 4, thorough discussion on the correlation of retinal vessel tortuosity with DR severity stages is provided in which the computation of vessels' tortuosity is dependent on the results of the vessels' segmentation. In Section 5, we provide the challenges and the future direction of diabetic retinopathy assessment in developing an automatic DR assessment system which associates retinal vessel tortuosity with DR severity stage. Finally, the conclusion of this paper is drawn in Section 6.

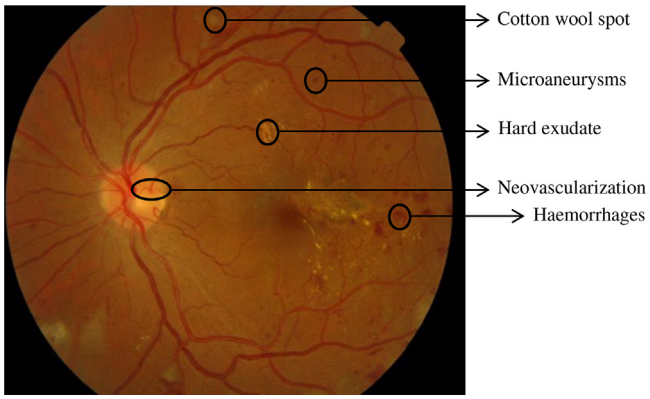

Fig. 1. Clinical features of diabetic retinopathy [3].

2. Diabetic retinopathy

DR is one of the microvascular complications arising from diabetes, which is a chronic condition associated with abnormally high blood sugar levels. All patients who have been diagnosed with diabetes, either type 1 or type 2, are at risk of developing DR. DR is a progressive disease of the retina that involves pathological changes of the blood vessels, and consequently results in the presence of one or more abnormal features recognisable by a trained observer. The common abnormal features seen on fundus images include microaneurysms, haemorrhages, hard exudates and cotton wool spots. Fig. 1 shows the abnormal features found in retinal fundus images of DR patients.

Aside of the presence of abnormal features, for the past decade, studies have been focusing on exploring the relationship between retinal vascular calibers and the risk of DR progression in diabetic patients [47,50–54]. In 2004, an initial study by Klein et al. demonstrated a positive relationship of arteriolar and venular caliber to the rate of DR progression [47,50]. Despite this, the findings were not supported by most of similar studies, based on [47,50,52,54], and the relationship between retinal venular caliber and the rate of DR progression is yet to be found. Nonetheless, in the experimental studies conducted randomly on diabetic patients, it was found that there were frequent increase of retina blood flow and the association of retinal arteriolar dilation in the retinas of diabetic patients [52]. However, in studies by Klein et al. [50] and Cheung at al [52], both agreed that there is an association between the retinal arteriolar caliber and the rate of DR progression. They used the same controlling risk factors, for example diabetes duration, glycaemic control, and blood pressure level. It can be concluded that there is strong evidence that may relate the retinal vascular caliber with the rate of DR progression in type 1 diabetic patients [47]. Then again, the collected data are not entirely consistent over time [47].

The progression of DR can be divided into several stages. First, as the blood glucose level increases, the permeability of the capillaries increases and there is a loss of elasticity of the endothelial capillary wall. This is the stage of mild nonproliferative diabetic retinopathy (NPDR). The appearance of microaneurysms is an early clinical sign of DR, which can be clinically seen as deep red spots varying from 15 μm to 60 μm in diameter [10]. Microaneurysms are basically the saccular outpouchings of the capillary wall, most likely due to the loss of retinal capillary pericytes and thickening of basement membrane. There is a continuous turnover of microaneurysms over time, and the rupture of microaneurysms can give rise to the formation of intraretinal haemorrhages, which are seen as small pin point (dot) red spots. Haemorrhages are sometimes indistinguishable from microaneurysms and they can be classified together as 'intraretinal red lesions'.