

# SphygmoCor and Diabetes Mellitus

Diabetes increases the risk of heart disease and stroke<sup>1</sup>, with heart disease being the leading cause of death. In addition, many people with Type 2 diabetes have co-existing risk factors, such as high blood pressure and high cholesterol<sup>3</sup>, further increasing their cardiovascular risk. Diabetes is also associated with long-term complications that affect almost every part of the body including heart and vessel disease, kidney failure, stroke, blindness, nerve damage and amputations. The SphygmoCor® system non-invasively provides measurements illustrating the progression of macrovascular disease driving the patient's risk of cardiovascular disease, thus providing a tool for assisting with early identification of high risk patients and subsequent management of the disease.

## Prevalence and Survival

In the United States, 20.8 million people are considered to have diabetes – 7% of the population. This consists of 14.6 million that have been diagnosed with diabetes and 6.2 million suspected of having diabetes that has not yet been diagnosed<sup>2</sup>. Each year, approximately 1.3 million people aged 20 years or older are diagnosed with diabetes and more than 60% of diabetics will die from heart disease<sup>1</sup>. Patients with Type 2 diabetes have a 2–7 times increased risk of cardiovascular mortality and morbidity<sup>4</sup> and patients with Type 1 diabetes also have an increased risk of cardiovascular disease<sup>5</sup>. Furthermore, diabetes has been reported to be one of the leading causes of end stage renal disease<sup>1</sup> which also carries an increased risk of cardiovascular disease<sup>6</sup>.

## Arterial Stiffness

The increased cardiovascular risk of patients with diabetes remains largely unexplained. Part of this increased risk relates to cardiovascular risk factors such as hypertension, dyslipidaemia, hyperglycaemia and obesity, but some of the increased risk appears to be independent of these factors and may be different for Type 1 and Type 2 diabetes.

Increased arterial stiffness has been associated with both Type 1<sup>7,8</sup> and Type 2 diabetes<sup>9,10,11</sup>, and may be a contributor to the high morbidity and mortality. The impact of this increased arterial stiffness on cardiovascular function can be examined by parameters provided by the SphygmoCor® system.

Peripheral pulse pressure, a surrogate marker for arterial stiffness, has been shown to be associated with Type 1 diabetes and compared with non-diabetics, age related blood pressure increases seem to shift to a 15–20 year younger age in Type 1 diabetes, suggesting accelerated vascular ageing<sup>5</sup>.

Aortic stiffness, as measured by aortic pulse wave velocity (PWV) has been shown to be an independent predictor of mortality in diabetic

patients, such that each increase of 1 m/s has an 8% increased risk of mortality<sup>10</sup>. Elevated aortic PWV and Aortic Augmentation Index (Alx) have been shown to be associated with Type 1 and Type 2 diabetes<sup>7,8,9,10,11</sup>.

Assessment of a cohort of patients in the FIELD (Fenofibrate Intervention and Event Lowering in Diabetes) Study showed a significant association between Augmentation Pressure (AP) and Alx and carotid IMT, an established marker of atherosclerosis, in Type 2 diabetics, suggesting that arterial stiffness may contribute to the accelerated atherosclerosis in Type 2 diabetes and that measures of central blood pressure and large artery stiffness may be superior to other conventional risk factors in determining the presence of vascular wall thickening in Type 2 diabetes<sup>4</sup>. A substudy of the FIELD investigation is ongoing and is expected to provide prospective data on the predictive values of AP and Alx for cardiovascular morbidity and mortality in Type 2 diabetic patients.

In previous studies, AP and Alx have also been shown to be strongly correlated with carotid IMT and plaque score in diabetic patients<sup>12,13</sup> and coronary artery disease<sup>14</sup>, the latter being commonly associated with diabetes. The CURES (Chennai Urban Rural Epidemiology Study) study showed that Type 2 diabetic patients with retinopathy had significantly higher Alx and IMT values than for those without retinopathy, suggesting an association between early atherosclerosis and diabetic retinopathy in Asian Indians, a high risk group for both diabetes and coronary artery disease<sup>13</sup>.

Children as young as 10 years old with Type 1 diabetes have also been observed to have increased arterial stiffness (Alx) when matched with control subjects<sup>15</sup>. This highlights the potential for markers of arterial stiffness such as those available from the SphygmoCor® system for providing additional information for cardiovascular risk stratification and optimisation of therapy in children with conditions such as Type 1 diabetes that have a high risk of developing cardiovascular and non-cardiovascular complications later in life.

With increased arterial stiffness, central systolic pressure increases resulting in an increase in cardiac workload and therefore myocardial demand. Increased arterial stiffness can contribute to the development and progression of hypertension, left ventricular hypertrophy and dysfunction and decrease in myocardial perfusion. The progression of these conditions is preventable and the use of key central cardiac function parameters provided by the SphygmoCor® system may assist with this. The SphygmoCor® Pulse Wave Analysis and Pulse Wave Velocity Systems allow for assessment of these important parameters of arterial stiffness, Alx and PWV. Once these conditions have developed, the system may assist with assessment of progression and the tailoring of drug therapies to the individual patient.

Decreases in arterial stiffness in patients with cardiovascular disease,

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including those with diabetes, have been demonstrated following pharmacological interventions, often independent of changes in cuff BP. Insulin is known to acutely decrease Alx independent of peripheral vascular resistance<sup>16,17</sup>, however this action is defective in insulin-resistant obese<sup>18</sup>, type 1<sup>18</sup> and type 2<sup>19</sup> diabetic patients. One study, however, has observed an improvement in Alx after six months of insulin therapy<sup>20</sup>. Among a number of pharmacological interventions shown to improve arterial stiffness, supplementation with oral ascorbic

acid has been shown to significantly lower Alx over a 4-week period in diabetic patients<sup>21</sup>. The SphygmoCor® system allows the physician to see the effects of their patient's treatment regimen through changes in the key central cardiac function parameters.

The SphygmoCor® system provides a clinically valuable cardiovascular risk assessment in these high-risk patients, enabling better informed treatment and patient management decisions.

## References

- National Institute of Diabetes and Digestive and Kidney Diseases. National Diabetes Statistics Fact Sheet: general information and national estimates on diabetes in the United States, 2003.
- National Institute of Diabetes and Digestive and Kidney Diseases. National Diabetes Statistics. NIH Publication No 06-3892 November 05.
- Williams B. The unique vulnerability of diabetic subjects to hypertensive injury. *J Hum Hypertens* 1999;13:S3-S8.
- Westerbacka J, Leinonen E, Salonen JT, *et al*. Increased augmentation of central blood pressure is associated with increases in carotid intima-media thickness in type 2 diabetic patients. *Diabetologia* 2005;48:1654-1662.
- Ronnback M, Fagerudd J, Forsblom C, *et al*. Altered age-related blood pressure pattern in Type 1 diabetes. *Circulation* 2004;110:1076-1082.
- U.S. Renal Data System, USRDS 2004 Annual Data Report: Atlas of End-stage renal disease in the United States. National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, MD, 2004.
- Brooks B, Molyneaux L, Yue DK. Augmentation of central arterial pressure in Type 1 diabetes. *Diabetes Care* 1999;22:1722-1727.
- Wilkinson IB, MacCallum H, Rooijmans DF, *et al*. Increased augmentation index and systolic stress in Type 1 diabetes mellitus. *QJM* 2000;93:441-8.
- Schram MT, Henry RMA, van Dijk AJM, *et al*. Increased arterial stiffness in impaired glucose metabolism and Type 2 diabetes. The HOORN study. *Hypertension* 2003;43:176-181.
- Cruickshank K, Riste L, Anderson SG, *et al*. Aortic pulse-wave velocity and its relationship to mortality in diabetes and glucose intolerance. *Circulation* 2002;106:2085-2090.
- Smith A, Karalliedde J, De Angelis L, Goldsmith D, Viberti G. Aortic pulse wave analysis and albuminuria in patients with Type 2 diabetes. *J Am Soc Nephrol* 2005;16:1069-75.
- Fukui M, Kitagawa Y, Nakamura N, *et al*. Augmentation of central arterial pressure as a marker of atherosclerosis in patients with Type 2 diabetes. *Diab Res Clin Pract* 2003;59:153-61.
- Rema M, Deepa R, Mohan V, Ravikumar R. Association of carotid intima-media thickness and arterial stiffness with diabetic retinopathy. *Diabetes Care* 2004;27:1962-1967.
- Weber T, Auer J, O'Rourke MF, *et al*. Arterial stiffness, wave reflections, and the risk of coronary artery disease. *Circulation* 2004;109:184-9.
- Haller MJ, Schwartz RF, Samyn M, *et al*. Radial artery tonometry demonstrates arterial stiffness in children with Type 1 diabetes. *Diabetes Care* 2004;27:2911-2917.
- Westerbacka J, Wilkinson I, Cockcroft J, *et al*. Diminished wave reflection in the aorta. A novel physiological action of insulin on large blood vessels. *Hypertension* 1999;33:1118-22.
- Westerbacka J, Seppala-Lindroos A and Yki-Jarvinen H. Resistance to acute insulin decreases in large artery stiffness accompanies the insulin resistance syndrome. *J Clin Endocrinol Metab* 2001;86:5262-8.
- Westerbacka J, Uosukainen A, Makimattila S, *et al*. Insulin-induced decrease in large artery stiffness is impaired in uncomplicated Type 1 diabetes mellitus. *Hypertension* 2000;35:1043-8.
- Tamminen M, Westerbacka J, Vehkavaara S, Yki-Jarvinen. Insulin-induced decreases in aortic wave reflection and central systolic pressure are impaired in Type 2 diabetes. *Diabetes Care* 2002;25:2314-9.
- Tamminen MK, Westerbacka J, Vehkavaara S, Yki-Jarvinen H. Insulin therapy improves insulin actions on glucose and aortic wave reflection in Type 2 diabetic patients. *Eur J Clin Invest* 2003;33:855-60.
- Mullen BA, Young IS, Fee H, McCance DR. Ascorbic acid reduces blood pressure and arterial stiffness in Type 2 diabetes. *Hypertension* 2002;40:804-9.

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