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Metabolic control of diabetes in a diabetes centre

一所糖尿病中心為患者進行的新陳代謝控制

Objective. To examine the effectiveness of a diabetes centre in restoring metabolic control in patients with poorly controlled diabetes.
Design. Retrospective review of medical records.
Setting. Diabetes centre of a district hospital, Hong Kong.
Participants. Patients with poorly controlled diabetes referred to a diabetes centre.
Main outcome measures. Primary endpoints were mean change in glycated haemoglobin levels and the number of patients who achieved glycated haemoglobin levels of 7.0% or lower, 7.5% or lower, and 8.0% or lower, respectively. Complementary endpoints were serial changes in body weight, blood pressure, and lipids.
Results. One hundred and eighty-five patients, predominantly with type 2 diabetes (94.6%), were reviewed. Median duration since diagnosis of diabetes was 8 years (interquartile range, 4.3-11.8 years). Seventy-three patients had a body mass index of 25 kg/m^2 or higher. The baseline and latest glycated haemoglobin levels were 10.4% (standard deviation, 2%) and 8.2% (1.4%), respectively; mean reduction was 2.2% (95% confidence interval, 1.9-2.5; P<0.0005). Eighty-one patients were discharged after a median 32 weeks of follow-up. Their mean glycated haemoglobin level on discharge was 7.5% (0.8%), and the mean reduction was 2.8% (95% confidence interval, 2.4-3.3; P<0.0005). The cumulative percentages of discharged patients who achieved glycated haemoglobin levels of less than 7.0%, 7.5%, and 8.0% were 30.9%, 53.1%, and 77.8%, respectively. Newly diagnosed diabetes (P=0.006) was the only factor which predicted a favourable glycaemic response.
Conclusion. The Diabetes Centre provided effective management for a heterogeneous group of patients referred with poorly controlled diabetes.

目的：研究一所糖尿病中心，為糖尿病控制不好的患者進行新陳代謝控制的成效。
設計：病歷紀錄的回顧。
安排：香港一所地區醫院的糖尿病中心。
參與者：糖尿病控制不好而被轉介到一所糖尿病中心的患者。
主要結果測量：主要指標是甘油酸化血色素水平的平均變化，及分別達至或低於7.0% ， 7.5% 和 8.0% 甘油酸化血色素水平的患者數目。輔助指標是體重、血壓和脂質的連續變化。
結果：回顧了185名主要患上第二型糖尿病(94.6%)的患者，他們糖尿病患的中值期為 8 年(四分位距， 4.3-11.8 年)。 73 名患者的體質指數達 25 kg/m^2 或以上。基線和最新的甘油酸化血色素水平分別為 10.4%(標準偏差， 2%)和 8.2% (1.4%)；平均減幅為 2.2% (95% 置信區間， 1.9-2.5；P<0.0005)。81名患者在為期32週的中值隨訪期後出院，他們出院時的平均甘油酸化血色素水平為 7.5% (0.8%)；平均減幅為 2.8% (95% 置信區間， 2.4-3.3；P<0.0005)。在出院患者中，達至甘油酸化血色素水平少於 7.0% ， 7.5% 和 8.0% 的累加百分比分別為 30.9% ， 53.1% 和 77.8% 。新診斷的糖尿病 (P=0.006)是唯一可預計對甘氨酸有良好反應的因素。
結論：糖尿病中心為糖尿病控制不好的不同類型的糖尿病轉介者提供了有效的治療。

Key words:
Diabetes mellitus;
Hemoglobin A, glycosylated;
Hong Kong;
Program evaluation

關鍵詞：
糖尿病；
使蛋白質糖基化的血色素 A；
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Introduction

The threat of a diabetes 'epidemic' is gaining momentum and arousing global concern. It is estimated that by the year 2050, developing countries, especially India and China, will contribute more than 75% of the diabetic population worldwide.[1] Optimal management of diabetes and its chronic complications thus represent a major challenge in an era of scarce resources. On average, one in 10 Hong Kong adults has diabetes, with many remaining undiagnosed.[2] This is in sharp contrast to the low prevalence in rural areas of Mainland China.[3] Improved socio-economic status and westernised, sedentary lifestyles play a role. Ageing, obesity, and a positive family history are independent predictive factors for the development of diabetes.[4] The increasing prevalence of young-onset type 2 diabetes due to the increased prevalence of childhood and adolescent obesity has also been recognised.[5] Prospective studies have not indicated a threshold level of glycated haemoglobin (HbA_{1c}) below which chronic complications do not occur.[6] Diabetic complications are a determining factor of the quality of life of patients.[7] The cost of diabetic care also increases greatly with the onset of complications. This suggests that substantial cost savings could be achieved if diabetic patients are maintained at a near-normal or the best possible level of glycaemia in order to delay the onset of complications.[8] Positive findings in clinical trial settings may not necessarily be translated into clinical benefits in real world settings, however.[9] Differences in population characteristics and the infrastructure of health care systems may influence the effectiveness and efficiency of care and result in variable outcomes.[10]

An organised management programme for diabetes is mandatory in order to optimise metabolic control of diabetes and the effective use of limited resources. Diabetes centres are designed to complement the deficiencies of traditional clinics in this regard.[11] Approximately 13 diabetes centres have been established in hospitals in Hong Kong. Regular audit is an integral part of any quality diabetic care programme.[12] It provides useful information for further improvement and development of local services. The Yan Chai Diabetes Centre is geographically detached from the specialist diabetes out-patient clinic, with a designated centre-based, diabetes nurse specialist responsible for daily management. We report a retrospective review of the metabolic control of diabetic patients currently receiving care in the Diabetes Centre.

Methods

Patient recruitment, follow-up, and data collection

Although there is no strict policy governing referral of patients to the Diabetes Centre, the most common reason for referral is poor diabetic control. During the period December 2000 to February 2001, all medical records for patients regularly attending the Diabetes Centre were scrutinised by researchers. Patients recruited were initially referred because of poor diabetic control, with an entry level of HbA_{1c} of more than 7.0%. This low cut-off for poor control was used because some patients may have high blood glucose levels despite HbA_{1c} levels of this magnitude. Patients were excluded if the follow-up duration was less than 3 months because HbA_{1c} had not been measured a second time. Patients who failed to attend the Diabetes Centre were routinely referred back to the referral source and were not included in this review. The attendance default rate was approximately 1% to 2% per month.

The selected cohort included patients referred at different times with different durations of follow-up. Some patients were discharged from the Diabetes Centre within the 3-month study period because of stable glycaemic control, while others continued to attend after this period. At each visit, patients were first interviewed by a nurse specialist to identify any care-related problems, either medical or social, before being assessed by the physician in charge. A joint discussion followed in which a management plan was formulated. Patients were encouraged to perform home blood glucose monitoring. If necessary, the nurse specialist would coordinate referrals to other specialists, including dietetic therapists and podiatrists. Telephone consultations with the nurse specialist were available during office hours. Between scheduled visits, follow-up of patients by the nurse specialist occurred at patients' requests, with adjustment of medication if necessary.

Patients were discharged if glycaemic control was considered optimal. In general, the aim was for near-normal glycaemic control although the individual target HbA_{1c} varied, especially with patients' age. Younger patients with type 1 diabetes and those with brittle diabetic control were retained for follow-up at the Diabetes Centre. Patients without complications were referred to the general diabetes out-patient clinic and continued to attend for annual review and screening for complications at the Diabetes Centre. Patients with more complex management needs were referred to the specialist diabetes clinic. Patients were arbitrarily classified as having newly diagnosed diabetes if they were seen within 12 months of initial diagnosis. Data collected included patient characteristics (sex, age, body weight, body mass index [BMI], and smoking status) and clinical information, including duration of follow-up, previous follow-up at the Diabetes Centre, duration and classification of diabetes, family history of diabetes involving first degree relative(s), and the presence of diabetic complications. A macrovascular complication was defined as the presence of any one of the following:

(1) hypertension;
(2) stroke, including transient ischaemic attack;
(3) coronary heart disease, with or without myocardial infarction; and
(4) peripheral vascular disease with or without amputation.

A microvascular complication was defined as the presence of any one of the following:

(1) diabetic retinopathy (any stage);
(2) diabetic neuropathy suggested by clinical examination, abnormal monofilament test (≥K; Smith & Nephew Rolyan Inc., Germantown, US), increased vibration thresholds (≥25 volts; Horwell Neurothesiometer, Nottingham, UK) in the feet, or nerve conduction tests; and
(3) diabetic nephropathy suggested by persistent macroalbuminuria or a creatinine level of more than 120 μmol/L (normal range, 60-120 μmol/L) not attributable to other known renal disease such as glomerulonephritis or renal artery stenosis.

Macroalbuminuria was defined as a urine albumin concentration of 300 mg/L or more (Albustix; Bayer Diagnostics, Bridgend Ind Estate, UK) in a random spot urine on more than one occasion, or a 24-hour urine albumin excretion of more than 300 mg/day. Microalbuminuria was diagnosed if two of three of the following were present: a random spot urine albumin concentration of 20 mg/L or more (Micral-Test; Roche, Mannheim, Germany); an albumin to creatinine ratio of 2.5 mg/mmol or more in an early morning urine sample; and a 24-hour urine albumin excretion of 30-300 mg/L. Serial measurements of body weight, BMI, blood pressure, total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-chol), and low-density lipoprotein cholesterol (LDL-chol) levels, in addition to HbA_{1c} levels were recorded. A hypoglycaemic episode was defined as minor if the attack did not require hospitalisation and as major if the attack resulted in hospitalisation. Hyperglycaemia requiring hospitalisation was also noted. Adjustments of diabetic treatment during follow-up in the Diabetes Centre were recorded.

Biochemical endpoints

The main biochemical endpoint was change in HbA_{1c} level during attendance at the Diabetes Centre. The baseline and latest HbA_{1c} levels were compared. The baseline HbA_{1c} levels were measured within the 3-month period prior to the first visit to the Diabetes Centre. The number of patients who achieved specific HbA_{1c} levels (≤7.0, ≤7.5, ≤8.0, >8.0%) by the end of the study period was also assessed. Analysis was performed for the study population as a whole, as well as for subgroups stratified according to specific criteria. These criteria included:

(1) whether they were discharged or current patients at the Diabetes Centre;
(2) newly diagnosed patients or known to have diabetes for more than 1 year;
(3) age-group (<35, 35-64, ≥65 years);
(4) duration of diabetes (<5, 5-9, ≥10 years); and
(5) BMI levels (<23, 23-24.9, 25-29.9, ≥30 kg/m^2).

Glycated haemoglobin levels were measured using high performance liquid chromatography (Variant HbA_{1c} program; BIO-RAD, Hercules, California, US) with a laboratory reference range of 4.5% to 6.5%. Serial changes in body weight, blood pressure, and lipids were considered complementary endpoints with respect to overall clinical and metabolic control.

Statistical analysis

Data were analysed for the study group as a whole and also by subgroups, as defined above. The number of patients (percentage of total), the mean (standard deviation [SD]), and the median (interquartile range [IQR]) for variables are reported where appropriate. For categorical variables, the statistical significance of an association was calculated using the Chi squared test. Comparison of repeated measurements on the same variable was made using the Student's *t* test for continuous parametric variables (body weight, BMI, systolic blood pressure [SBP] and diastolic blood pressure [DBP], HbA_{1c}, TC, HDL-chol, LDL-chol) and the Wilcoxon signed rank test for continuous non-parametric variables (TG). Comparison of two independent samples was done by independent samples *t* test for continuous parametric variables (body weight, BMI, HbA_{1c}, TC, HDL-chol, LDL-chol) and Mann-Whitney test for continuous non-parametric variables (TG). Repeated measures analysis of variance (ANOVA) were used to compare serial changes in HbA_{1c} levels among different subgroups of patients (age, duration of disease, and BMI). In the univariate correlation analysis, Pearson correlation coefficients were used for continuous parametric variables (BMI, HbA_{1c}, SBP, DBP, TC, HDL, LDL) and Spearman rank order correlation coefficients were used if at least one continuous non-parametric variable was involved (TG, age, and duration of diabetes). In the multivariate analysis, a multiple linear regression model was used to examine the association of BMI with clinical and biochemical parameters. The threshold level of significance was P=0.05 (two-tailed). At least 80 patients were needed in order to have a study power of 80% for detecting a 0.9% change in HbA_{1c}. This was based on the assumption that the SD of HbA_{1c} in poorly controlled diabetic patients was 2.0%. The Statistical Package for the Social Sciences (Macintosh version 10.0; SPSS Inc., Chicago, US) was used.

Results

A total of 282 patients were screened between 1 December 2000 and 28 February 2001. Of these, 185 patients met the inclusion criteria and their medical records were reviewed. The median duration of follow-up was 41 weeks (IQR, 24-64.5 weeks). Most patients (94.6%) had type 2 diabetes. The majority (157; 84.9%) were referred by the hospital diabetes clinic. Twenty-one (11.4%) patients were referred directly from wards upon discharge. Seven (3.8%) patients who had attended the Diabetes Centre previously and had been discharged to the general diabetes out-patient clinic demonstrated a deterioration in glycaemic control during annual review for diabetic complications at the Diabetes Centre. Forty-three (23.2%) patients had attended the Diabetes Centre in the past. Eighty-one (43.8%) patients were discharged within the study period; all but one had type 2 diabetes. The median duration of follow-up at the Diabetes Centre for discharged patients was 32 weeks (IQR, 22-52 weeks). Patients were seen at an average interval of approximately 5.2 weeks. Twenty patients were discharged

to the general out-patient clinic. Others were discharged to the specialist diabetes clinic. Table 1 summarises patients' biographical, clinical, and biochemical characteristics. Patient ages ranged from 18 to 77 years (median, 57.5 years). Sixty percent belonged to the 35 to 64 years age-group. Females slightly outnumbered male patients (female: male=1.2:1). Forty percent of patients were either current or previous smokers. A positive family history of diabetes was noted for 38.5%.

Thirty-three (17.8%) patients had newly diagnosed diabetes and most were seen at the Diabetes Centre within 6 months of diagnosis. This group was comparatively younger than known diabetic patients (median age, 41 versus 59 years; P<0.0005). Most (75%) patients had the disease for at least 5 years and 39% of diabetic patients had the disease for 10 years or more. The median duration of disease for known diabetic patients was 8 years (IQR, 4.3-11.8 years).

No difference was found between male and female patients in BMI levels (mean, 24.4 kg/m^2). Using the Asian standards,[13] approximately 20% and 30% of patients were overweight (BMI, ≥23 kg/m^2) and obese (BMI, ≥25 kg/m^2), respectively. Twenty (10.8%) patients had severe obesity (BMI, ≥30 kg/m^2). Macrovascular and microvascular complications were present predominantly in known diabetic patients. Forty percent of patients had co-existing hypertension. The mean SBP of known diabetic patients was

Table 1. Patient characteristics and baseline clinical and biochemical measurements

	Patients, n=185	New, n=33	Known, n=152	P value*
Sex (M/F)	83/102	18/15	65/87	0.217
Age (years)				
Range	18-77	18-70	19-77	
Median (interquartile range)	57.5 (42-65)	41 (31-52)	59 (46.3-66)	<0.0005
Age-group (years)†				
<35	25 (13.5%)	10 (30.3%)	15 (9.9%)	0.004
35-64	108 (58.4%)	18 (54.5%)	90 (59.2%)	
≥65	52 (28.1%)	5 (15.2%)	47 (30.9%)	
Mean body weight (SD) [kg]	62.1 (13.6)	63.1 (14.5)	62 (13.4)	0.659
Body mass index (kg/m^2)				
Range	12.3-39.5	17.2-32.8	12.3-39.5	
Mean (SD)	24.4 (4.4)	23.8 (4.0)	24.5 (4.5)	0.374
Body mass index group†‡				
<23	69 (37.9%)	13 (39.4%)	56 (37.6%)	0.795
23-24.9	40 (22.0%)	8 (24.2%)	32 (21.5%)	
25-29.9	53 (29.1%)	10 (30.3%)	43 (28.9%)	
≥30	20 (11.0%)	2 (6.1%)	18 (12.1%)	
Mean systolic blood pressure (SD) [mm Hg]	134 (23)	123 (22)	137 (23)	0.002
Mean diastolic blood pressure (SD) [mm Hg]	75 (10)	73 (10)	76 (10)	0.091
Smoking status†				0.894
Current/ex-smoker	75 (40.5%)	14 (42.4%)	61 (40.1%)	
Never	109 (58.9%)	18 (54.5%)	91 (59.9%)	
Data not available	1 (0.5%)	1 (3.0%)	0 (0%)	
Duration of diabetes mellitus (years)				
Median (interquartile range)	NA§	NA	8 (4.3-11.8)	
<5†	NA	NA	38 (25.0%)	
5-9†	NA	NA	56 (36.8%)	
≥10†	NA	NA	58 (38.2%)	
Treatment at entry†				<0.0005
Diet only	12 (6.5%)	11 (33.3%)	1 (0.7%)	
Single OHA‖	48 (25.9%)	10 (30.3%)	38 (25.0%)	
Combination OHAs	74 (40.0%)	4 (12.1%)	70 (46.1%)	
Insulin ± OHAs	51 (27.6%)	8 (24.2%)	43 (28.3%)	
Macrovascular complication†				
Hypertension	75 (40.5%)	3 (9.1%)	73 (48.0%)	<0.0005
Cardiovascular/cerebrovascular	21 (11.4%)	0 (0%)	21 (13.8%)	0.23
Microvascular complication†				
Retinopathy	74/175 (42.3%)	2/30 (6.7%)	72/145 (49.7%)	<0.0005
Neuropathy	36/171 (21.1%)	0/30 (0%)	37/141 (26.2%)	<0.007
Nephropathy	59/184 (32.1%)	2/33 (6.1%)	57/151 (37.7%)	<0.0005
Microalbuminuria†	17/83 (20.5%)	3/21 (14.3%)	14/62 (22.6%)	0.416
Macroalbuminuria†	57/184 (31.0%)	2/33 (6.1%)	55/151 (36.4%)	0.001
Median creatinine (interquartile range) [μmol/L]	73 (57-87)	70 (54-82)	73 (58-93)	0.157
Creatinine level >150 μmol/L†	12 (6.5%)	0 (0%)	12 (7.9%)	-
Mean total cholesterol (SD) [mmol/L]	5.2 (1.3)	4.9 (1.1)	5.3 (1.4)	0.185
Median triglycerides (interquartile range) (mmol/L)	1.3 (0.9-2.2)	1.3 (0.6-1.5)	1.4 (0.9-2.4)	0.049
Mean high-density lipoprotein cholesterol (mmol/L)	1.18 (0.41)	1.28 (0.45)	1.16 (0.40)	0.218
Mean low-density lipoprotein cholesterol (mmol/L)	3.2 (0.9)	3.1 (0.7)	3.2 (0.9)	0.838
Mean baseline glycated haemoglobin (SD)	10.4 (2.0)	11.4 (2.7)	10.2 (1.7)	0.017

* All P values are referring to comparisons of newly diagnosed with known patients
† Percent of total are given in brackets
‡ Body mass index values were missing for three patients
§ NA not applicable
‖ OHA oral hypoglycaemic agent

significantly higher than that of the newly diagnosed patients (137±23 versus 123±22 mm Hg; P=0.002), but not for mean DBP [70±10 versus 73±10 mm Hg; P=0.091]. Coexisting cerebrovascular or coronary heart disease was present in 11.4% of patients at baseline. Four patients had documented peripheral vascular disease, including two with amputation of limbs. Diabetic retinopathy, neuropathy, and nephropathy were documented in approximately 40%, 20%, and 30% of patients, respectively. Proteinuria was present in 74 patients, including 17 patients with documented microalbuminuria. Twelve known diabetic patients had creatinine levels exceeding 150 μmol/L. Known diabetic patients had marginally higher TG levels than newly diagnosed diabetic patients (P=0.049). No difference was seen in other lipid parameters.

Glycaemic control

Table 2 summarises the changes in HbA_{1c} levels for all patients as well as the predefined subgroups. The baseline and latest mean HbA_{1c} levels for all patients were 10.4% and 8.2%, respectively. Overall, HbA_{1c} levels decreased by 20%, equivalent to a mean change of 2.2% (95% confidence interval [CI], 1.9-2.5) during the study period (P<0.0005). As expected, a greater reduction was seen for patients who were discharged. The latest achieved mean HbA_{1c} level of discharged patients was 7.5% (SD, 0.8%). The cumulative percentages of patients who achieved the latest HbA_{1c} levels of less than 7.0%, 7.5%, and 8.0% were 18.9%, 34.6%, and 53.0%, respectively. Similar figures for discharged patients were 30.9%, 53.1%, and 77.8%, respectively. Newly diagnosed diabetic patients had both higher baseline (11.4% versus 10.2%) and lower latest HbA_{1c} levels (7.7% versus 8.3%) than known diabetic patients (P<0.0005 for both comparisons). Similarly, fewer known diabetic patients had achieved an HbA_{1c} level of 7.5% or less (30% versus 60%, P=0.006).

Reductions in HbA_{1c} levels were not associated with patients' age or duration of diabetes (Table 2). Although the absolute number of patients who achieved lower HbA_{1c} levels did decrease with increasing age and duration of diabetes, this difference did not reach statistical significance. Patients in the higher BMI range had a smaller reduction in HbA_{1c} levels (P=0.039). This difference was not significant, however, after the exclusion of type 1 diabetic patients from the analysis (P=0.053). In addition, the percentage of patients who achieved any particular HbA_{1c} level did not appear to differ across different BMI groups (P=0.990). In the univariate analysis, the latest HbA_{1c} level achieved was not shown to be associated with patients' age, duration of diabetes, or initial BMI level.

At the end of the study period, 80% of patients had received an increase in medication, either dose titration of existing therapy or the addition of new drug(s). Eleven of 12 patients who were initially using diet alone for diabetic control required medication. The use of combination oral hypoglycaemic agents (OHAs) for newly diagnosed diabetic patients increased from 12.1% to 30.3%. At the same time, the use of combination oral drug therapy for known

Table 2. Summary of changes in glycated haemoglobin levels in all patients and according to predefined patient subgroups

Patients (subgroups)	Glycated haemoglobin level (%)				
	Patients No.	Baseline Mean (SD)	Latest Mean (SD)	Mean change (95% CI)	P value
Total	185	10.4 (2.0)	8.2 (1.4)	2.2 (1.9-2.5)	*
New	33	11.4 (2.7)	7.7 (1.7)	3.7 (2.7-4.7)	*
Known	152	10.2 (1.7)	8.3 (1.3)	1.9 (1.5-2.2)	*
					<0.0005†
Discharged	81	10.3 (1.9)	7.5 (0.8)	2.8 (2.4-3.3)	*
Current patients	104	10.5 (2.1)	8.8 (1.5)	1.7 (1.2-2.2)	*
					<0.0005†
Type 1 diabetes	10	11.1 (2.6)	8.5 (2.0)	2.6 (1.0-4.3)	0.006
Type 2 diabetes	175	10.3 (1.9)	8.2 (1.4)	2.2 (1.8-2.5)	*
					0.439†
Duration groups (years)‡	152				
<5	38	10.1 (1.8)	8.2 (1.5)	1.9 (2.7-4.7)	*
5-9	56	10.2 (1.7)	8.4 (1.4)	1.9 (1.4-2.4)	*
≥10	58	10.1 (1.7)	8.3 (1.2)	1.8 (1.3-2.3)	*
					0.988†
Age-groups (years)					
<35	25	10.3 (2.3)	8.2 (1.6)	2.1 (1.0-3.1)	*
35-64	108	10.3 (2.0)	8.2 (1.5)	2.1 (1.6-2.5)	*
≥65	52	10.7 (1.7)	8.2 (1.2)	2.5 (1.9-3.0)	*
					0.549†
Body mass index groups (kg/m²)§	182				
<23	69	10.9 (2.1)	8.4 (1.6)	2.5 (2.0-3.1)	*
23-24.9	40	10.2 (1.8)	7.9 (1.2)	2.3 (1.5-3.0)	*
25-29.9	53	9.9 (1.8)	8.1 (1.3)	1.8 (1.2-2.3)	*
≥30	20	10.1 (1.6)	8.3 (1.4)	1.8 (0.6-3.2)	0.005
					0.039†‖

* P <0.0005
† Repeated measures ANOVA for subgroup effect on glycated haemoglobin reduction
‡ Known diabetes only
§ Body mass index values were missing in three patients
‖ P=0.053 after the exclusion of type 1 diabetes

Table 3. Summary of changes in body weight, blood pressure, and lipid profile of patients during follow-up at the Diabetes Centre

	Baseline	Latest	Mean changes (95% CI)	P value
Mean body weight (SD) [kg]	62.1 (13.6)	63.5 (13.1)	1.4 (0.8-1.9)	<0.0005
Mean body mass index (SD) [kg/m^2]	24.4 (4.4)	24.9 (4.1)	0.5 (0.3-0.83)	<0.0005
Mean systolic blood pressure (SD) [mm Hg]	134 (23.3)	128 (18.9)	6.5 (3.7-9.4)	<0.0005
Mean diastolic blood pressure (SD) [mm Hg]	75 (10.2)	75 (7.8)	0.3 (-1.2–1.8)	0.704
Mean total cholesterol (SD) [mmol/L]*	5.5 (1.4)	5.0 (0.9)	0.5 (0.3-0.7)	<0.0005
Median triglyceride (interquartile range) [mmol/L]*	1.3 (0.9-2.2)	1.2 (0.8-2.0)	NA†	0.007
Mean high-density lipoprotein cholesterol (SD) [mmol/L]*	1.26 (0.48)	1.24 (0.44)	0.01 (-0.06–0.09)	0.74
Mean low-density lipoprotein cholesterol (SD) [mmol/L]*	3.4 (1.0)	3.2 (0.8)	0.2 (-0.1–0.5)	0.143

* There were 104/101/49/49 pairs of total cholesterol/triglyceride/high-density lipoprotein cholesterol/low-density lipoprotein cholesterol, respectively
† NA not applicable

diabetic patients decreased from 46.1% to 29.6%. This was due to an increase in the number of patients receiving insulin therapy alone or in combination with OHAs (from 28.3% to 60.5%). Medication use by the remaining 20% of patients either did not change or decreased. Improved glycaemic control, with or without hypoglycaemia, was the most common reason for reducing medication. These patients included two who were initially thyrotoxic and became euthyroid during follow-up at the Diabetes Centre. More than 95% of patients were performing self-monitoring of blood glucose (SMBG) at home; most (70%) were newly taught SMBG at the Diabetes Centre. Forty (21.6%) patients had at least one documented minor or major hypoglycaemic attack during their follow-up at the Diabetes Centre. Most of these patients (n=31) were using insulin therapy and there were four major attacks (2.2%). All patients made a full recovery. Three patients were admitted to hospital for hyperglycaemia during their follow-up at the Diabetes Centre.

Body weight, blood pressure, and lipids

Table 3 summarises the changes in body weight, blood pressure, and lipid profile of patients attending the Diabetes Centre. An average weight gain of 2.3% was observed at the conclusion of this study, equivalent to a mean incremental weight gain of 1.4 kg (95%CI, 0.8-1.9; P<0.0005). Only insulin-treated patients gained a significant amount of weight—an average of 2.2 kg (95% CI, 1.4-3.0) corresponding to a 3.6% increase (P<0.0005). Patients taking metformin, sulphonylurea, and combination OHAs showed a mean gain of 0.2 kg, 0.4 kg, and 0.2 kg, respectively. Systolic blood pressure decreased by an average of 6.5 mm Hg (95% CI, 3.7-9.4; P<0.0005). No significant change in DBP was evident. Fifty percent of patients were taking antihypertensive drugs at the end of the study period. The mean TC level decreased by 0.5 mmol/L (P<0.0005), whereas the median TG level decreased by 0.1 mmol/L (P=0.007). There were only 49 pairs of HDL-chol and LDL-chol measurements available for analysis. The HDL-chol values were seen to rise and the LDL-chol values to fall but these changes did not reach statistical significance. Seventeen percent of patients were taking lipid-lowering agents; two thirds of these were receiving statins as treatment. In the univariate analysis, the latest BMI level was positively correlated with DBP and TG level and inversely correlated with HDL-chol level. When these three factors were analysed in a multiple linear regression model, only the correlations with DBP (B=0.135; SE=0.055; 95% CI, 0.025-0.244; t=2.449; P=0.016) and HDL-chol (B=-3.38; SE=1.071; 95% CI, - (5.509-1.251); t=-3.155; P=0.002] were significant.

Young-onset type 2 diabetes

Thirty-eight patients in the cohort had disease onset at the age of 35 years or younger. These included 10 patients with type 1 presentation, leaving 28 patients clinically classified as having young-onset type 2 diabetes. There was a strong association with family history of diabetes (63.0% versus 33.3%; P=0.008) and obesity (60.7% versus 38.3%, P=0.008) in this patient subgroup. Patients with young-onset type 2 diabetes had lower SBP values at baseline (119 versus 139 mm Hg; P<0.0005) and at latest measurement (120 versus 131 mm Hg; P<0.0005) and latest TC levels (4.9 versus 5.1 mmol/L; P=0.023) compared with older diabetic patients.

Patients with severe obesity

Twenty patients had BMI levels at or more than 30 kg/m^2, including five of 35 kg/m^2 or more. Nine of these patients were female. Their median age was 44 years (range, 19-73 years). All had type 2 diabetes, including six patients with young-onset type 2 diabetes (≤35 years). Thirteen (65%) patients had a positive family history of diabetes. Their baseline and latest HbA_{1c} (mean) levels were 10.1% and 8.3%, respectively, which were comparable to the whole study population. These patients tended to have higher baseline TG (median, 1.7 mmol/L; range, 0.6-5.5 mmol/L) and lower HDL-chol levels (mean, 0.98 mmol/L; SD, 0.4 mmol/L) but these differences were not statistically significant. Thirteen patients required insulin therapy; all had concurrent OHAs. All but one were taking metformin, with or without insulin or sulphonylurea. Patients taking insulin therapy gained an average of 1.9 kg (2.3%) during the study period.

Discussion

The results confirm that attendance at the Diabetes Centre was effective in restoring metabolic control in this heterogeneous group of poorly controlled diabetic patients. The clinical and metabolic profiles of all patients also improved, as indicated by the modest reductions in TC and TG levels, and lowered SBP. At the end of the study period, the mean

HbA_{1c} levels had decreased by 20%. Eighty-one patients, with a mean HbA_{1c} level of 7.5%, were discharged from the Diabetes Centre during the 3-month period after a median follow-up of 7 months. One in four patients was discharged to a diabetes out-patient clinic in the primary health care sector. In keeping with Chan et al,[14] this study demonstrates that the Diabetes Centre facilitated the transfer of diabetic patients with stable disease to the primary care sector.

Although most recent guidelines on diabetes management have recommended a target HbA_{1c} level of less than 7.0%,[12,15] these guidelines have been largely based on studies using an upper normal limit (UNL) for HbA_{1c} assays of 6.0%. Using 1.1xUNL and 1.3xUNL to define the ideal and unsatisfactory levels for HbA_{1c}, as suggested in Hong Kong guidelines,[16] the corresponding thresholds in our laboratory would be less than 7.2% and 8.5% or more, respectively. Eighty percent of discharged patients had an HbA_{1c} level of 8.0% or less, which suggests that this is a realistic and achievable target for such a patient group. For younger diabetic patients, however, near-normalisation of HbA_{1c} level should remain the goal.[17] Newly diagnosed diabetes was the only factor in this cohort that predicted a favourable outcome in terms of glycaemic control. This might partly be explained by the correction of initial glucose toxicity, which has been shown to cause both pancreatic islet-cell dysfunction and increased peripheral insulin resistance.[18] Furthermore, newly diagnosed diabetic patients in this cohort were younger, appeared to be better educated, and may have differed in their motivation to achieve diabetic control.

In this study, age of diabetic patients and duration of diabetes had no significant effect on glycaemic control achieved. Prospective trials have shown that glycaemic control deteriorates over time as a result of progressive beta-cell failure and the eventual inadequacy of monotherapy.[19] Nevertheless, our findings show that with intensified therapy,[20] improvements in glycaemic control can be seen in most patients with type 2 diabetes. A diabetes centre can facilitate the administration of intensified therapy to poorly controlled diabetic patients. Notwithstanding the doubtful beneficial effect of aggressive glycaemic control in elderly diabetic patients, the number of elderly diabetic patients in our society is increasing and they should not be denied access to quality diabetic care. Education is an essential element for diabetes management.[21] An important advantage of the Diabetes Centre over a traditional diabetes clinic is the provision of greater time and space for patient care, and the use of full-time nurse specialists. The patient environment provided by a diabetes centre is more conducive to learning,[11] while the importance of a nurse specialist for diabetes care was recognised as early as the 1940s.[22] Local experience has also shown that a well-trained diabetes nurse contributes significantly to the care of diabetic patients.[23] Increased attention offered in this setting might in itself have contributed to improvements in glycaemic control.[24] More than 95% of patients attending the Diabetes Centre were completing SMBG, compared with only 40% of patients attending the diabetes clinic. It has been suggested that glycaemic control might improve due to increased awareness of hyperglycaemia by patients, but this was not confirmed by a recent meta-analysis of the clinical efficacy of diabetic self-monitoring.[25,26] The current study showed that improvement in glycaemic control did not necessarily equate to an increase in drug therapy. Twenty percent of patients improved without an increase in medication. As both a resource centre and a clinic, the diabetes centre thus appears invaluable for the management of inadequately controlled diabetes.

The majority of patients attending the Diabetes Centre have type 2 diabetes, and many have multiple cardiovascular risk factors (CVRF) including hypertension, dyslipidaemia, hyperuricaemia, abnormal haemostasis, and central obesity. A multiple risk factor approach addressing all CVRFs is therefore mandatory for the management of diabetic patients. Intensive blood pressure control has been shown to reduce macrovascular complications more than glycaemic control alone.[27] Insulin resistance has been postulated as the underlying key pathophysiological mechanism linking multiple CVRFs.[28] A local study, however, has suggested that obesity might have a greater effect than insulin resistance.[29] The finding of increasing BMI in patients with type 2 diabetes and increasing hypertension and adverse lipid profiles in this study reiterates the importance of weight control. Even modest weight loss (7%-10%) has been shown to benefit control of glycaemia in diabetes.[30] A greater number of patients in the higher BMI ranges in this study required insulin (data not shown). This suggests that obese diabetic patients might experience more problems with insulin resistance. Nevertheless, optimal glycaemic control can be achieved, even for very obese patients.

The pathogenesis of young-onset type 2 diabetes is heterogeneous, and multiple genetic defects have been described.[31,32] A positive family history and obesity are more common among these patients. We found similar results in our younger cohort of patients with type 2 diabetes. In addition, patients with severe obesity (BMI $\geq$30 kg/m^2) tended to be younger and have a stronger family history for diabetes. It is likely that both environmental (obesity) and genetic factors are important in the pathogenesis of young-onset type 2 diabetes. Study results showed that only 30% to 40% of young patients achieved HbA_{1c} levels of 7.5% or less, suggesting room for improvement in managing this patient group. Weight gain and hypoglycaemia are known disadvantages of intensive glycaemic control, particularly with the use of insulin.[6,33] This study showed that insulin-treated patients experienced the greatest weight gain and risk of hypoglycaemia. The absence of significant weight gain in other patients, however, might reflect the relatively small sample size and the short duration of follow-up.

The limitations of this study include the relatively small number of patients and the quality of the data

gathered. The content and intensity of therapy received by each patient, and their compliance were not controlled in this retrospective review. More importantly, the use of HbA_{1c} levels alone as an outcome measure would appear inadequate. The impact of a diabetes centre on long-term clinical outcomes needs further study. Moreover, a follow-up study is indicated to document how many patients sustain good metabolic control after discharge from the Diabetes Centre.

Conclusion

Patients with poorly controlled diabetes, regardless of age and duration of diabetes, may benefit from referral to a diabetes centre. A diabetes centre provides a platform for a multi-faceted approach to diabetes management. Factors that may have contributed to the success of diabetic control achieved by the Diabetes Centre include: increased patient education, increased interaction between patient and care providers, increased attention, and increased self-monitoring. The Diabetes Centre also facilitated the use of intensified treatment in patients with persistently poor control, and the discharge of patients with stable disease to community level care. Obesity in this patient group was associated with a greater prevalence of hypertension and adverse lipid profiles, emphasising the importance of a holistic approach to the management of diabetes. Overall, patients referred to the Diabetes Centre were shown to have a 20% reduction in HbA_{1c} level during their period of follow-up at the centre.

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