

Letters to the Editor

Diastolic abnormalities might precede systolic abnormalities of left ventricular function in Type 1 (insulin-dependent) diabetes mellitus

Dear Sir,

Thuesen et al. [1] recently reported on an increased myocardial contractility in Type 1 diabetic patients which was related to the state of metabolic control. They used echocardiography to measure left ventricular fractional shortening and mean circumferential shortening velocity to assess myocardial function. Left ventricular performance depends on intrinsic myocardial contractility, preload and afterload. Both echocardiographic parameters are affected by loading conditions. No differences in left ventricular diastolic diameters compared with controls were noted by the authors. Therefore, no differences in preload might be assumed. On the other hand, an increase in cardiac output was observed in diabetic patients, despite a similar mean arterial pressure. Therefore, peripheral vascular resistance has to be lower in the diabetic study group. This might account for the increase in fractional shortening and mean circumferential shortening velocity. We therefore suggest that poor metabolic control in diabetic patients alters loading conditions by decreasing afterload. Whether intrinsic myocardial contractility is enhanced remains to be established.

In addition, we performed an echocardiographic study on well controlled Type 1 diabetic patients with a similar mean duration of disease (8 ± 6 years) without evidence of significant diabetic microangiopathy [2]. Our study group consisted of 50 Type 1 diabetic patients (26 ± 8 years), educated and treated as previously described [3]. Long-term metabolic control was assessed throughout 12 months by multiple HbA_{1c} measurements; one-third had HbA_{1c} values in the range of nondiabetic subjects. No significant difference in left ventricular systolic performance could be observed when well-controlled Type 1 diabetic patients were compared with age- and sex-matched nondiabetic controls [2]. A significant prolongation of the isovolumetric relaxation period, reflecting an early diastolic event, could be demonstrated even in diabetic patients with HbA_{1c} concentrations in the physiologic range. Therefore, systolic performance of the left ventricle in short-term Type 1 diabetic patients with near normoglycemia might be normal, although subtle alterations of diastolic function might already be present.

Yours sincerely,
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Increased myocardial contractility and improved glycaemic control

Dear Professor Berger,

We were interested to read the recent report by Thuesen et al. [1], in which the authors demonstrated that increased myocardial contractility was reduced with improved glycaemic control in 8 newly diagnosed or poorly controlled Type 1 (insulin-dependent) diabetic patients. However, as their patients had significant metabolic disturbance, presumably factors such as dehydration, hypovolaemia, hyperdynamic circulation, increased levels of circulating catecholamines, altered peripheral resistance and venous return would be present to a greater or lesser degree. The haemodynamic effect of these factors would be sufficient to explain the abnormal echocardiographic findings, and it would not be surprising to find that these improved significantly when such factors were corrected. Similar echocardiographic abnormalities would be found in any patient subject to similar haemodynamic insults, and cannot be considered to be a specific finding in diabetes.

We have also recently reported studies in recently diagnosed Type 1 diabetic patients using nuclear angiography, and have demonstrated marked variation in left ventricular function in recently diagnosed patients compared with stable diabetic patients when the measurements are repeated [2]. In our subjects, the initial studies were done at a time when the metabolic and circulatory abnormalities associated with recently diagnosed diabetes had been corrected. We would, therefore, agree with Thuesen et al. [1] that, during conditions of poor metabolic control, abnormalities of left ventricular function may be discovered and these may be reversible with improvement of control.

In the larger group of 24 diabetic patients, there is a considerable overlap with the control group for the values of left ventricular fractional shortening. Like the mean circumferential shortening velocity, this is a derived variable and may be significantly affected by heart rate. As the diabetic group had a higher heart rate, which is not discussed or explained, this could contribute to the observed differences between the groups. In both their patient groups, the abnormal echocardiographic findings could be explained by extra cardiac factors such as changes in circulating fluid volume, catecholamine secretion, peripheral resistance, venous return, and so on. Normalisation would be expected if these factors were related to poor diabetic control and could be corrected by improved control.

Their study demonstrates an expected physiological response of the myocardium to stress factors such as indicated above, and does not imply any specific abnormality in diabetic patients.

Yours sincerely,
A. D. B. Harrower

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Reply from the authors

Dear Professor Berger,

We appreciate the comments by Dr. Harrower on our paper [1]. We fully agree that haemodynamics in Type 1 (insulin-dependent) diabetic patients during conditions of standard, and especially during conditions of poor, metabolic control is influenced by several factors, and that similar echocardiographic abnormalities are likely to be found in patients suffering from diseases other than diabetes. The important thing, however, is that haemodynamic abnormalities seem to be reversible with correction of the metabolic disturbances seen in diabetes, as also reported by Mathiasen et al. [2]. These findings seem completely compatible with the above-mentioned results from Dr. Harrower's group.

On the other hand, we do not agree that the demonstrated cardiac hypercontractility demonstrated in the 24 diabetic patients during conditions of standard metabolic control is merely a function of increased heart rate. Mean circumferential shortening velocity is certainly influenced by heart rate, which is closely related to ejection time, but left ventricular fractional shortening is not.

We accept that increased myocardial contractility is an expected physiological response of the myocardium to stress factors and, therefore, fully agree that the findings reported by no means are specific to diabetes mellitus. However, as also discussed in the paper [1], we find that hypercontractility can be found in Type 1 diabetic patients during ordinary 'out-patient' metabolic conditions. Therefore, it can be considered a part of everyday life, and might be of clinical relevance, since haemodynamic changes are likely to play an important part in the development of diabetic microvascular disease.

Yours sincerely,
L. Thuesen and J. Sandahl Christiansen

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Abnormal identification of the sweet taste of D-glucose anomers

Dear Sir,

Several physiological processes triggered by D-glucose, such as the stimulation of insulin secretion or the inhibition of glucagon release, display anomeric specificity, with α -D-glucose being more efficient than β -D-glucose [1, 2]. In the islet cells, the anomeric specificity of the secretory response is thought to be secondary to the higher rate of utilization of α - as distinct from β -D-glucose, as recently reviewed in this journal [3]. The α -anomer of D-glucose was also reported to taste sweeter than the β -anomer [4]. A perturbation of the latter hierarchy in an otherwise normal subject is reported here.

Normal and diabetic subjects were asked to taste three iced solutions containing either no glucose or each of the two anomers dissolved in water immediately prior to the test at a concentration of 4 g/dl. The latter concentration was selected on the basis of 20 preliminary trials in which normal subjects were invited to taste iced solutions containing increasing concentrations of equilibrated D-glucose (nil, 0.6, 1.2, 1.8, 2.5 and 5.0 g/dl). The perception of a sweet taste was usually achieved at a concentration of 1.2 g/dl (13 cases) or more (7 cases). However, up to 1.8 g/dl, the establishment of a graded response was often doubtful. This was never the case in the range between 1.8 and 5.0 g/dl. Fifteen normal subjects, 6 males and 9 females, 25 to 57 years old, all members of our laboratory staff, identified α -D-glucose as sweeter than β -D-glucose when tested on one (7 cases), two (6 cases) or three (2 cases) separate occasions, with only 3 hesitant responses in a total of 25 trials. One member of our staff, a normal female aged 42, identified β -D-glucose as sweeter than α -D-glucose on five distinct occasions over a period of one year. On three of these occasions, 2 to 4 iterative trials were performed, and opposite results were also encountered. Thus, in this subject, the hierarchy in the sweet taste of D-glucose anomers was considered to be absent, if not reversed. Her two sons were also tested twice during each of two separate interviews. The oldest son (12 years) identified α -D-glucose as sweeter all 4 times, whilst the youngest son (10 years) did so in 3 out of 4 trials.

Since diabetes mellitus is proposed to represent a disorder of the α -stereospecific glucoreceptor [4], 23 diabetic subjects from the diabetes outpatient clinic, including 9 males and 14 females, aged 19 to 82 years, were also examined each on only one occasion. Seventeen subjects [8 Type 1 (insulin-dependent) and 9 Type 2 (non-insulin-dependent) patients] identified α -D-glucose as sweeter than β -D-glucose. Three patients, aged 30 to 57, provided a faltering answer; 3 other patients, aged 57 to 73, selected β -D-glucose as the sweetest anomer. These 6 patients included 3 Type 1 and 3 Type 2 diabetic patients. It would thus appear that the normal anomeric preference in taste is often preserved in diabetic patients. However, considering the size of both the normal and diabetic samples, as well as the differences in age and cultural status between these two groups, we feel it premature to elaborate on the precise incidence of anomeric preferences in healthy and diabetic subjects. Nevertheless, the knowledge that certain persons may fail to identify the sweeter taste of the α -