A New Classification Plot for the C-Peptide Suppression Test

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ABSTRACT

Context and objective To evaluate the C-peptide suppression test as a screening test in patients with symptoms of hypoglycemia as compared to the standard fasting test.

Design Retrospective discriminant analysis of data from C-peptide suppression tests.

Setting Clinical study.

Patients Two different sets: patients with insulinomas and patients without insulinomas but having symptoms compatible with hypoglycemia.

Interventions The results from C-peptide suppression tests of 26 patients with insulinomas and 100 patients without insulinomas were compared.

Main outcome measures A classification plot which introduces two discriminant parameters for the C-peptide suppression test: the ratio of [blood glucose]/[C-peptide] at the lowest C-peptide concentration and mean glycemia during insulin infusion.

Results In patients with insulinomas, minimal serum C-peptide levels were higher (1.81±0.87 ng/mL; median 1.83 ng/mL; maximal suppression 37±24% of basal C-peptide levels) as compared to patients without insulinoma (0.40±0.15 ng/mL; median 0.30 ng/mL; maximal suppression of 75±9%; P<0.001). Mean glycemia during the test was lower in patients with insulinomas (30.8±3.3 *vs.* 47.5±8.3 mg/dL; P<0.001) as was the [blood glucose]/[C-peptide] ratio (21.9±14.6 *vs.* 139.2±43.8; P<0.001). Discriminant analysis revealed a specificity of 96% to rule out the diagnosis of 'insulinoma' at a 1% probability threshold with a sensitivity of 100%.

Conclusions We developed a new classification plot for the C-peptide suppression test in order to accurately identify those patients whose symptoms of hypoglycemia are not due to endogenous hyperinsulinemia/insulinomas. Thus, the need for fasting tests and hospitalization costs can be reduced.

INTRODUCTION

The supervised standard fasting test is the classical endocrinological test procedure of choice in any patient suspected of having hypoglycemia. This can be explained by the test's sensitivity and specificity of almost 100% [1, 2, 3, 4, 5]. Since the patient has to be taken care of in case of hypoglycemic episodes, the fasting test should be performed in a hospital setting. An additional mandatory prerequisite is the careful and laborious processing of the blood samples in order to obtain reliable biochemical data for evaluation. These data are needed especially when the diagnosis of endogenous hyperinsulinemia/insulinoma seems to be less probable despite the patient's presentation of clinical symptoms. This scenario has fuelled the search for a simpler, less expensive and less time consuming test procedure than the fasting test but one which is equally valid. Such a test would reduce the frequency of hospitalization due to fasting tests ordered for the mere exclusion of endogenous

hyperinsulinemia. It was Service *et al.* [6] who first published normative data for the C-peptide suppression test. The rationale of this test is based upon the physiological suppressibility of endogenous insulin secretion as is the standard fasting test. However, this is carried out by means of an exogenous insulin infusion, not by fasting [7, 8, 9, 10, 11, 12]. The idea of a normative approach was important as the results of other suppressive test maneuvers had revealed the heterogeneity of the beta-cell response in patients with endogenous hyperinsulinemia/insulinomas [13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24]. Although in the study by Service *et al.* [6], the influence of gender, age, and body mass index were carefully assessed in a large number of patients by means of stepwise multiple regression analysis, criteria for the diagnosis of endogenous hyperinsulinemia/insulinoma were only developed in eight of these patients.

We present herein new data generated from the C-peptide suppression test which demonstrate a sensitivity of 100% and a specificity of 96% for the exclusion of excessive endogenous hyperinsulinemia. We used linear discriminant analysis and developed a two-dimensional graphical plot so that patients with insulinomas are clearly separated from patients without insulinomas at probability thresholds of 1%, 5%, and 10%. Consequently, those patients who definitely require a supervised fasting test are identified. In addition, those patients in whom autonomous excessive insulin secretion can be excluded due to completely normal suppression of C-peptide are easily screened.

METHODS

Study Design and Patients

For the study, two different sets of data were available: 50 patients with insulinomas (Group A) and 174 healthy people (Group B). In all patients of Group A (50/50, A1), endogenous hyperinsulinemia had already been proven biochemically by means of a supervised standard fasting test. Of this group, 26 patients gave their informed consent for an additional second test prior to surgery, the C-peptide suppression test (26/50, Group A2). Group B consisted of patients who had either complained of unspecific postprandial adrenergic symptoms or who had presented measurements of low blood glucose levels of unknown origin. One hundred patients of this group had been studied by means of a C-peptide suppression test (100/174, Group B2) and 74 patients had taken part in a standardized fasting test (74/174, Group B1). Unfortunately, only 3 people from Group B2 had agreed to additionally take part in a 72 hour fasting test. This meant that it was less likely to develop a cross-over or even a prospective study design with a sufficient number of patients within an acceptable period of time. Therefore, we decided to retrospectively analyze the data available for patients with insulinomas versus those without insulinomas with reference to discriminant criteria: 1) during the C-peptide suppression test (Groups A2 and B2), and 2) during the standardized fasting test (Groups A1 and B1). The clinical characteristics of all patients concerning age, gender and body mass index are summarized in Table 1.

Table 1. Clinical characteristics of the patients.

	C-peptide suppression test			Standardized fasting test		
	Insulinoma (A2; n=26)	No Insulinoma (B2; n=100)	P value	Insulinoma (A1; n=50)	No Insulinoma (B1; n=74)	P value
Gender						
Female/Male	18/8	65/35	0.863	32/18	53/21	0.484
Age (years)						
Mean±SD	52.1±15.3	38.5±14.2	<0.001	50.9±14.6	40.2±15.2	<0.001
Median (range)	51 (32-82)	36 (14-70)		51 (16-82)	37 (17-78)	
Body mass index (BMI; kg/m²)						
Mean±SD	27.3±4.0	23.2±3.6	<0.001	26.3±3.8	24.6±4.4	0.028
Median (range)	26.9 (20.1-38.4)	22.6 (17.1-34.6)		25.8 (19.7-38.4)	24.1 (16.6-39.4)	

C-Peptide Suppression Test

The test was started in the morning (8:00-9:00 AM) after an overnight fast. Only the patients with previously proven endogenous hyperinsulinemia (Group A2) were allowed to have a carbohydrate containing drink at 3:00 AM in order to avoid a morning fasting glucose level below 40 mg/dL. Two teflon catheters were inserted into the antecubital veins of each arm and kept patent by saline infusions (0.156 mol/L). Regular insulin (0.075 IU/kg/h, Actrapid HM®, Novo-Nordisk, Bagsvaerd, Denmark), diluted with saline and mixed with 1 mL of the patients' whole blood in order to avoid adsorption of diluted insulin to the tubing materials, was infused at a rate of 15 mL/h for 120 minutes. In patients with insulinomas, the insulin dose was reduced to 0.05 IU/kg/h when the patients presented a fasting blood glucose level of less than 50 mg/dL. Blood samples were taken from the controlateral catheter at timepoints of -15, 0, 20, 40, 60, 80, 100, 120, 135, and 150 minutes in order to determine concentrations of blood glucose and serum C-peptide levels. In 13 out of 26 patients with proven insulinomas, the test had to be prematurely terminated due to symptoms of neuroglycopenia.

Supervised Standard Fasting Test

Fasting tests started in the morning at 9:00 AM with the ingestion of 100 g of glucose. Blood samples were drawn at regular intervals for the determination of blood glucose, serum insulin and serum C-peptide until termination of the test due to biochemical hypoglycemia or until 72 hours had elapsed.

Analytical Methods

Blood glucose levels were measured immediately with a Beckman Glucose Analyzer (Beckman Instruments, Fullerton, CA, USA).

Serum C-peptide concentrations were assayed by means of radioimmunoassay (RIAgnost HC-Peptid, Behring-Werke, Marburg, Germany). The coefficients of variation (CV) for precision were 8% for low (0.8 ng/mL) and 6% for high (7.5 ng/mL) serum levels. The intra-assay CV was 10% and the limit of detection was 0.3 ng/mL. Recovery (0.9-7.5 ng/mL added to serum) was 102% (CV 8%) and linearity (serum dilution 1:1 to 1:4) was 98% (CV 7 %). The normal fasting range of the assay in normal subjects was 0.5-2.5 ng/mL.

Serum insulin concentrations were assayed by means of radioimmunoassay (RIA100, Pharmacia Co., Erlangen, Germany). Precision was 13% for low (3 μU/mL) and 5% for high (90 μU/mL) serum levels. The intra-assay CV was 9% and the limit of detection was 3 μU/mL. Recovery (1.5-60 μU/mL added) was 96% (CV 9%) and linearity was 99% (CV 5%). Cross-reactivity with human proinsulin was 40% and with C-peptide was less than 0.2%. The normal fasting range of the assay in normal subjects was 4.0-10.0 μU/mL.

ETHICS

The study was performed in accordance with the guidelines of the declaration of Helsinki.

DATA ANALYSIS

C-Peptide Suppression Test

Mean values of blood glucose and C-peptide concentrations, the ratio of blood glucose and C-peptide, the reverse C-peptide/blood glucose ratio and the percentage of maximal C-peptide suppression were calculated and evaluated for optimal classification of 26 patients with insulinomas (Group A2) and 100 patients without insulinomas (Group B2). For these calculations, the data of these 126 patients were pooled. Log transformation (ln, base e) had to be applied in order to normalize the data.

The highest classification accuracy was empirically found for the following parameters allowing a two-dimensional linear discrimination ratio: 1) [blood glucose]/[C-peptide] at low C-peptide (BG/CP), and 2) mean blood glucose concentrations (MBG). The ratio was calculated from the blood glucose concentration (mg/dL) measured at the time of the lowest C-peptide concentration (ng/mL) and plotted as the natural logarithm (ln, base e) on the y-axis. C-peptide concentrations below the detection limit of 0.3 ng/mL were not used in the BG/CP-ratio calculation; instead, they were set to 0.3 ng/mL Thus, an exponential increase of the BG/CP-ratio was limited. The BG/CP-ratio rather than the reverse CP/BG-ratio was used to avoid very small numbers with negative values after logarithmic transformation.

Mean blood glucose concentrations (MBG) during the C-peptide suppression test were calculated between 40 and 150 minutes or in patients with an insulinoma from 40 minutes until the termination of the test and plotted as the natural logarithm (ln, base e) on the x-axis.

Supervised Standard Fasting Test

During the fasting test, the MBG was derived from measurements obtained regularly until termination of the test or until 72 hours had elapsed. The ratio of blood glucose and C-peptide levels was calculated at the lowest C-peptide level measured during the test.

DISCRIMINANT ANALYSIS

By application of stepwise discriminant analysis, the two parameters, ln MBG and ln BG/CP, were finally chosen for the development of discriminant functions. Due to the low number of observations, the simplest method, namely linear discriminant analysis, was used. Probability thresholds (T) of 0.10, 0.05, and 0.01 were used in the decision rule, e.g. the decision 'no insulinoma' was made only if the probability of insulinoma was less than 10, 5, or 1%.
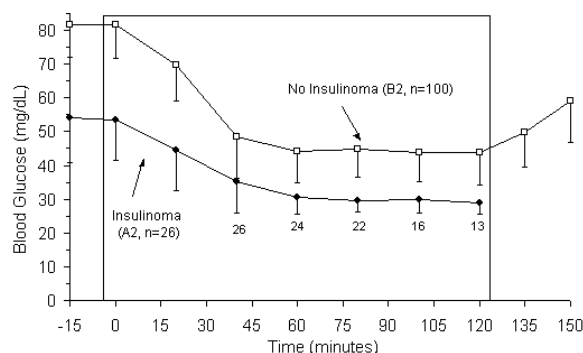

Figure 1. Blood glucose (mg/dL) in patients with insulinoma (closed circles with index of number of patients; Group A2) and patients without insulinoma (open squares; Group B2) during the C-peptide suppression test. Insulin was infused from 0 to 120 minutes as indicated by the box. All values are mean±SD.

Data are given as mean±standard deviation (SD) or as the median and range.

STATISTICAL METHODS

The procedures STEPDISC and DISCRIM of the SAS Institute [25] were used for computational analysis. The Student's two-tailed group t-test and the Yates' corrected X-squared test were applied for statistical comparisons between groups. A two-tailed P value of 0.05 was chosen to detect statistically significant results.

RESULTS

C-Peptide Suppression Test

In patients with an insulinoma (Group A2), blood glucose concentrations declined from a baseline level of 54.0±13.0 mg/dL (range 32.5-78.5 mg/dL) to 30.4±5.0 mg/dL (range 20.0-36.0 mg/dL) within 60 minutes of insulin infusion (Figure 1). In 13 of the 26 patients, the test had to be terminated at the end of the 2 hour insulin infusion period due to the development of neuroglycopenic symptoms. C-peptide levels (Figure 2) declined from 2.93±1.02 ng/mL (range 1.19-6.40 ng/mL) to a mean of 1.47±0.78 ng/mL (range 0.60-2.80 ng/mL) after 120 min accounting for a mean C-peptide suppression
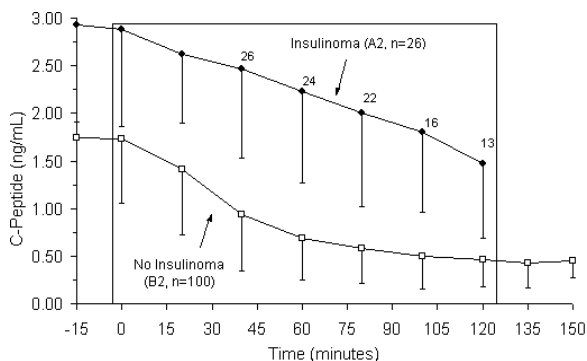
Figure 2. Serum C-peptide concentration (ng/mL) in patients with insulinoma (closed circles with index of number of patients; Group A2) and patients without insulinoma (open squares; Group B2) during the C-peptide suppression test . Insulin was infused from 0 to 120 minutes as indicated by the box. All values are mean±SD.

of 45±24% (Figure 3). The absolute mean of minimal C-peptide concentrations in all 26 patients was 1.81±0.87 ng/mL (median 1.83; range 0.60-3.41 ng/mL) resulting in a maximal percentage decrease of C-peptide of 37±24% (median 35%, range 0-80%). As shown in Figure 4, the mean ratio of [blood glucose]/[C-peptide] in patients with an insulinoma did not change significantly from the basal value of 19.9±8.0 and remained constant at ratios between 16.9±9.5 (60 min) and 26.8±16.0 (120 min).

In symptomatic patients without an insulinoma (Group B2), blood glucose concentrations declined from a baseline level
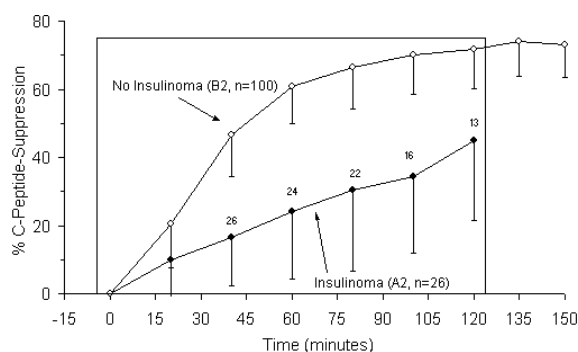
of 81.5±9.4 mg/dL (range 59.0-106.5 mg/dL) to 44.1±9.2 mg/dL (range 30.0-87.5 mg/dL) within 60 minutes (Figure 1). C-peptide levels declined from 1.75±0.67 ng/mL (range 0.63-3.97 ng/mL) to a mean of 0.45±0.18 ng/mL (range 0.30-1.04 ng/mL) after 2 hours of insulin infusion (Figure 2). The absolute mean of minimal C-peptide concentrations was 0.40±0.15 ng/mL (median 0.30; range 0.30-0.91 ng/mL). The maximal percentage decrease of C-peptide was 75±9% (median 78 %; range 45-91%; P<0.001 *vs.* patients with insulinoma). The mean ratio of [blood glucose]/[C-peptide] increased from a basal value of 54.0±24.7 to 110.1±41.9 at the end of insulin infusion (Figure 4; P<0.001 *vs.* patients with insulinoma). The data for the mean glycemia (MBG) during the test period and the ratio of [blood glucose]/[C-peptide] at the lowest C-peptide level in both patient groups are summarized in Table 2 and Figure 5.

Linear discriminant analysis revealed a sensitivity of 100% (95% CI: 86.8-100%) and a specificity of 96.0% (95% CI: 90.1-98.9%) at a probability threshold of T=0.05 (96 out of 100 patients) for the decision 'no insulinoma'. The mathematical function of the discrimination line (5%) was as follows: ln BG/CP = 6.681 - (0.697 x ln MBG). The results of the probability thresholds T=0.01 and T=0.1 were: specificity 96.0% (95% CI: 90.1-98.9%) and sensitivity 100% (95% CI:

Figure 3. Percent inhibition of basal C-peptide in patients with insulinoma (closed circles with index of number of patients; Group A2) and patients without insulinoma (open squares; Group B2) during the C-peptide suppression test . Insulin was infused from 0 to 120 minutes as indicated by the box. All values are mean±SD.
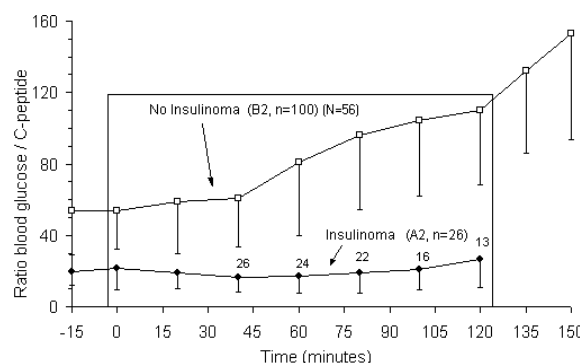

Figure 4. [Blood glucose]/[C-peptide] ratio in patients with insulinoma (closed circles with index of number of patients; Group A2) and patients without insulinoma (open squares; Group B2) during the C-peptide suppression test . Insulin was infused from 0 to 120 minutes as indicated by the box. All values are mean±SD.
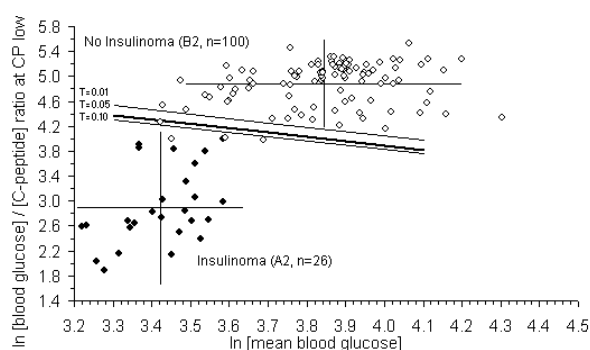
Figure 5. Mean blood glucose *vs*. [blood glucose]/[C-peptide] ratio at lowest C-peptide concentration from C-peptide suppression test.

Data are plotted as a natural logarithm (ln) in patients with insulinoma (closed circles; Group A2, n=26) and patients without insulinoma (open circles; Group B2, n=100).Mean values±2 SD are indicated for both groups. The lines represent the discriminant criteria for the possibility thresholds T=0.01, 0.05, and 0.10.

86.8-100%) at a threshold of 0.01 (1%; ln BG/CP = 6.831 - (0.697 x ln MBG)); specificity 97.0% (95% CI: 91.5-99.4%) and sensitivity 100% (95% CI: 86.8-100%) at a threshold of 0.10 (10%; ln BG/CP = 6.612 - (0.697 x ln MBG); Figure 5).

Supervised Standard Fasting Test

The mean age and the BMI of 50 patients with insulinoma (Group A1) and 74 patients without insulinoma (Group B1) subjected to a fasting test were comparable to the patients subjected to the C-peptide suppression test (Table 1). The fasting test data (duration of the fast, glucose nadir, serum insulin and

serum C-peptide levels at blood glucose nadir) are summarized in Table 3.

The data for the mean blood glucose concentrations (MBG) during the test period and the ratio of [blood glucose]/[C-peptide] at the lowest C-peptide level in both patient groups are summarized in Table 4 and Figure 6. The discriminant function (threshold 0.05, 5%) yielded a specificity of 97.3% (72/74 patients) and a sensitivity of 100%. The mathematical function for the discriminant line was as follows: ln BG/CP = 12.048 - (2.030 x ln MBG).

DISCUSSION

With a diagnostic sensitivity and specificity of nearly 100%, the supervised prolonged fasting test is the most specific and sensitive suppression test to confirm the diagnosis of excessive endogenous insulin secretion or its absence, respectively [1, 2]. The availability of a simpler test to be used in an outpatient unit for patients unlikely to be suffering from endogenous hyperinsulinemia but complaining of symptoms compatible with underlying hypoglycemia would reduce the requirement of fasting tests.

The C-peptide suppression test is based on the exogenously induced suppression of C-peptide secretion rather than endogenously induced suppression of insulin and C-peptide levels during fasting [7, 10, 11, 12, 26, 27]. Service *et al.* [6] published normative data for the C-peptide suppression test (insulin dosage

Table 2. Mean blood glucose concentrations (MBG), ratio of blood glucose/C-peptide ([BG]/[CP] ratio) at the time of lowest C-peptide concentration and maximal percent suppression of C-peptide in patients with insulinoma (Group A2) and without insulinoma (Group B2) during a C-peptide suppression test (ln=natural logarithm, base e).

C-peptide suppression test	Insulinoma (A2, n=26)	No Insulinoma (B2, n=100)	P value
Mean blood glucose (MBG; mg/dL)			
Mean±SD	30.8±3.3	47.5±8.3	<0.001
Median (range)	31.1 (25.0-36.0)	48.1 (30.6-73.9)	
ln MBG (mean±SD)	3.42±0.11	3.85±0.18	
Ratio blood glucose/C-peptide [BG; mg/dL]/[CP; ng/mL]			
Mean±SD	21.9±14.6	139.2±43.8	<0.001
Median (range)	15.1 (6.6-54.1)	145.0 (53.4-253.3)	
ln ratio (mean±SD)	2.90±0.61	4.88±0.36	
Maximal C-peptide suppression (%)			
Mean±SD	37.1±23.9	75.4±9.4	<0.001
Median (range)	34.8 (0-80.3)	78.3 (45.0-91.3)	

Table 3. Duration of fasting test, blood glucose nadir and simultaneous serum insulin and serum C-peptide levels in patients with insulinoma (Group A1) and healthy patients without insulinoma (Group B1)

	Insulinoma (A1, n=50)	No Insulinoma (B1, n=74)	P value
Duration (hours)			
Mean±SD	18.4±10.0	72	-
Median (range)	15.3 (7.5-48.0)	-	
Glucose nadir (mg/dL)			
Mean±SD	30.7±5.7	52.7±10.9	<0.001
Median (range)	31.0 (18.0-41.0)	51.0 (36.0-86.0)	
Insulin levels at glucose nadir (μU/mL)			
Mean±SD	23.3±23.9	5.1±2.9	<0.001
Median (range)	14.8 (5.2-145.0)	3.8 (3.0-17.4)	
C-peptide levels at glucose nadir (ng/mL)			
Mean±SD	2.60±1.18	0.63±0.32	<0.001
Median (range)	2.44 (0.91-7.40)	0.57 (0.30-1.93)	

0.125 U/kg/h) in 101 healthy lean and obese subjects. Increasing age and BMI attenuated the suppression of C-peptide in age and weight matched patients. The percent of the decrease of C-peptide, rather than the absolute C-peptide concentrations, was found to be the most reliable indicator of abnormal responses. In our study, absolute C-peptide concentrations (Figure 2) and percent inhibition of baseline C-peptide concentrations (Figure 3) in patients with and without insulinoma clearly overlap at the level of 1 SD. This is a well known problem of C-peptide suppression test data when a single parameter is used for a one-dimensional discrimination. Furthermore, patients with insulinomas demonstrate considerable heterogeneity as to absolute insulin levels, secretory patterns of insulin secretion and C-peptide response during suppression tests [16, 20, 22]. Consequently, the C-peptide response during the C-peptide

suppression test may vary to a great extent. However, near-normal C-peptide levels which may occur in the presence of hypoglycemic blood glucose levels, seem to be
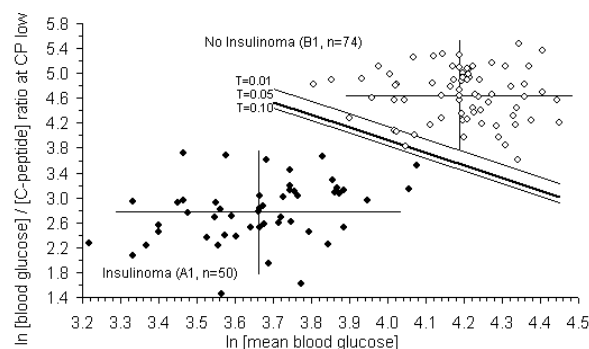

Figure 6. Mean blood glucose *vs.* [blood glucose]/[C-peptide] ratio at lowest C-peptide concentrations from fasting tests.

Data are plotted as a natural logarithm (ln) in patients with insulinoma (closed circles; Group A1, n=50) and patients without insulinoma (open circles; Group B1, n=74). Mean values±2 SD are indicated for both groups. The lines represent the discriminant criteria for the possibility thresholds T=0.01, 0.05, and 0.10.

Table 4. Mean blood glucose concentrations (MBG) and ratio of blood glucose/C-peptide ([BG]/[CP] ratio) at the time of lowest C-peptide concentration in patients with insulinoma (Group A1) and without insulinoma (group B1) during a fasting test (ln=natural logarithm, base e).

Fasting Test	Insulinoma (A1, n=50)	No Insulinoma (B1, n=74)	P value
Mean blood glucose (MBG; mg/dL)			
Mean±SD	39.6±7.4	66.6±9.9	<0.001
Median (range)	39.4 (25.0-58.9)	66.6 (44.9-99.6)	
ln MBG (mean±SD)	3.66±0.19	4.19±0.15	
Ratio blood glucose/C-peptide [BG; mg/dL]/[CP; ng/mL]			
Mean±SD	18.1±8.9	113.9±47.8	<0.001
Median (range)	16.8 (4.3-41.3)	106.0 (36.7-238.4)	
ln ratio (mean±SD)	2.78±0.50	4.63±0.43	

inappropriately high reflecting impaired suppression at the prevailing degree of hypoglycemia [6]. This relationship can mathematically be taken into account by the introduction of a [blood glucose]/[C-peptide] ratio calculated at the lowest C-peptide concentration. Thus, the discriminatory power of a single parameter plotted vertically is greatly amplified and reduces the overlap. We have introduced a second discriminant parameter, the integrated mean glycemia during insulin infusion, in order to separate the two groups of subjects along the horizontal axis of the discriminant plot analysis. Using the classification plot (Figure 5) individual patients can be identified as to who should definitely undergo a fasting test to confirm the absence of autonomous insulin secretion.

In order to test the plausibility and accuracy of the new discriminant criteria introduced for the exclusion of autonomous insulin secretion, we have retrospectively calculated the same parameters from the fasting tests performed diagnostically in patients with and without insulinomas. As shown in Table 4 and Figure 6, there is an almost identical range of the [blood glucose]/[C-peptide] ratio with a discriminant sensitivity of 100% and a specificity of 97%. Therefore, a reliable relationship between C-peptide and blood glucose during both tests, independent of the conditions used in order to suppress insulin secretion by exogenous insulin infusion or endogenously during a fast is obvious. It should be emphasized, however, that a prospective study would be necessary to compare C-peptide levels during fasting tests and C-peptide suppression tests between the same patients.

The C-peptide suppression test, conveniently performed in an outpatient setting, may serve as a reliable tool to screen those patients with symptoms of hypoglycemia who require a standard fasting test. Our intention is not to replace this most powerful and accurate diagnostic tool by the C-peptide suppression test to prove or exclude endogenous hypersecretion of insulin. Instead, in our study, we sought to refine the diagnostic procedure for the many patients with symptoms compatible with hypoglycemia. Due to the laborious and cost-intensive disadvantages of the fasting test, we have increasingly noticed attempts to replace the careful biochemical evaluation simply by even more cost-intensive imaging procedures, a policy we would strictly discourage [28, 29]. Sensitivity rates in the range of 90-100% as published for the dynamic computed tomography and the endoscopic ultrasonography [30, 31] were only obtained in studies including patients with proven insulinomas. Controlled studies have not been performed in which patients without pancreatic tumors were included.

In conclusion, by means of the [blood glucose]/[C-peptide] ratio and the mean glycemia during a C-peptide suppression test we have established criteria for the discrimination of normal subjects and patients with hyperinsulinemia due to excessive autonomous insulin secretion. With a specificity of 96% and a sensitivity of 100%, the C-peptide suppression test identifies those patients who definitely require a standard fasting test. The C-peptide suppression test may be used as a simple diagnostic tool to exclude patients with autonomous insulin secretion and, thus, reduce the hospitalization required for standard fasting tests.

Abbreviations BG/CP ratio: blood glucose/C-peptide ratio; CP/BG ratio: C-peptide/blood glucose ratio; MBG: mean blood glucose concentration

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