SUPPLEMENTARY DATA

Supplementary Material 1. Statistical methods used to conduct power calculations.

Post-hoc power calculations and patient numbers needed to detect changes were conducted considering (i) the observed partial correlations (Tables S4, S5) and (ii) for defined clinically relevant changes of the dependent variables (Tables S6, S7). In Tables S4 and S5, patient numbers to detect significant differences based on the observed partial correlations for a power of 80% were calculated. Additionally, the actual power of the partial correlations as observed in each set of analysis in our sample was determined. In Tables S6 and S7, patient numbers needed to detect significant changes with a power of 80% and the actual power for the given number of patients were calculated based on the observed residual standard deviation of the respective independent variable, the respective dependent variable, and a defined clinically relevant change of the respective dependent variable. Clinically relevant changes were defined as an absolute change of 0.5% for HbA_{1c} and of 0.1%/min for glucose disappearance rate and a relative change of 10% for C-peptide secretion capacity from glucagon stimulation test, ACPRG, $iAUC_{CP}$, and iBCF. Clinically relevant changes for HbA_{1c} were defined based on findings of the UK Prospective Diabetes Study Group (UKPDS) that a reduction in mean HbA_{1c} by 0.5% associated with a reduction in risk of 10.5% for any endpoint related to diabetes in patients with type 2 diabetes (1). A change in the homeostasis model assessment of insulin resistance (HOMA-IR), insulin sensitivity index (S_i), and acute insulin response (AIR) during the natural course of type 2 diabetes between 12 and 35% during 5.2 years of follow-up served as reference for the clinically relevant change of insulin sensitivity and secretion (2).

SUPPLEMENTARY DATA

Supplementary Table S1. Description of biospecimen handling and laboratory analyses.

	HbA_{1c}	Glucose	C-peptide
Biospecimen type	EDTA whole blood	Whole blood	Serum from whole blood with clot activator
Storage duration until analysis	0-6 h	n/a[†]	<1 week
Storage temperature	RT	RT	+6°C or -20°C
Freeze-thaw cycles before analysis	n/a	n/a	0
Assay	Variant-II (Bio-rad, Munich, Germany)	Glucose oxidase method (ecoSolo-II, Care Diagnostica, Voerde, Germany and EKF biosen C-Line glucose analyzer, EKF diagnostic GmbH, Barleben, Germany)*	Immulite chemiluminescence assay (Siemens, Erlangen, Germany)
Intra-assay CV (%)	<1	3.6/1.7	2.0
Inter-assay CV (%)	<1	<5/3.8	3.5
Measurement range (for undiluted samples)	n/a as analyzer has automated dilution system at certain range		n/a as analyzer has automated dilution system at certain range
Comments	measured according to the DCCT method yielding %-values which were then used to calculate mmol/mol data	-	-

*ecoSolo-II, Care Diagnostica, Voerde, Germany: 09/2005 – 02/2009. EKF biosen C-Line glucose analyzer, EKF diagnostic GmbH, Barleben, Germany: 03/2009-current. [†]Glucose was measured with a quality assured point of care testing (POCT) method from venous whole blood (3).
n/a, not applicable; RT, room temperature (20-25°C).

SUPPLEMENTARY DATA

Supplementary Table S1. Description of biospecimen handling and laboratory analyses (contd.).

	Triglycerides	HDL-cholesterol	LDL-cholesterol
Biospecimen type	Serum from whole blood with clot activator	Serum from whole blood with clot activator	Serum from whole blood with clot activator
Storage duration until analysis	0-6 h	0-6 h	0-6 h
Storage temperature	RT	RT	RT
Freeze-thaw cycles before analysis	n/a	n/a	n/a
Assay	Enzymatic assay on Hitachi 912 (Roche Diagnostics, Mannheim, Germany) or Modular P system (Roche Diagnostics, Mannheim, Germany)	Enzymatic assay on Hitachi 912 (Roche Diagnostics, Mannheim, Germany) or Modular P system (Roche Diagnostics, Mannheim, Germany)	Calculated using Friedewald equation
Intra-assay CV (%)	<1/1.1	<1/1.9	n/a
Inter-assay CV (%)	2.2/4.2	2.2/3.5	n/a
Measurement range (for undiluted samples)	n/a as analyzer has automated dilution system at certain range	n/a as analyzer has automated dilution system at certain range	n/a
Comments	-	-	-

n/a, not applicable; RT, room temperature (20-25°C).

SUPPLEMENTARY DATA

Supplementary Table S1. Description of biospecimen handling and laboratory analyses (contd.).

	hsCRP	IL-6	IL-18
Biospecimen type	Serum from whole blood with clot activator	Serum from whole blood with clot activator	Serum from whole blood with clot activator
Storage duration until analysis	Baseline 3.25-6.5 yrs 2-Y-FU 0.4-4.3 yrs	Baseline 3.25-6.5 yrs 2-Y-FU 0.4-4.3 yrs	Baseline 3.25-6.5 yrs 2-Y-FU 0.4-4.3 yrs
Storage temperature	-80°C	-80°C	-80°C
Freeze-thaw cycles before analysis	0	1	1
Assay	Roche/Hitachi c 311 analyzer (Basel, Switzerland)	Quantikine HS ELISA (R&D Systems, Wiesbaden, Germany)	IL-18 ELISA (MBL, Nagoya, Japan)
Intra-assay CV (%)	1.9	6.0	6.5
Inter-assay CV (%)	3.9	12.2	12.1
Measurement range (for undiluted samples)	n/a as analyzer has automated dilution system at certain range	0.156 – 10 pg/ml	10.24 – 1000 pg/ml
Comments	-	All samples were measured undiluted and yielded values within the measurement range.	All samples were measured at 1:5 dilution and yielded values within the measurement range.

hsCRP, high-sensitivity C-reactive protein; IL, interleukin; n/a, not applicable.

SUPPLEMENTARY DATA

Supplementary Table S1. Description of biospecimen handling and laboratory analyses (contd.).

	sE-Selectin	sICAM-1
Biospecimen type	Serum from whole blood with clot activator	Serum from whole blood with clot activator
Storage duration until analysis	Baseline 3.25-6.5 yrs 2-Y-FU 0.4-4.3 yrs	Baseline 3.25-6.5 yrs 2-Y-FU 0.4-4.3 yrs
Storage temperature	-80°C	-80°C
Freeze-thaw cycles before analysis	1	1
Assay	Quantikine ELISA (R&D Systems, Wiesbaden, Germany)	Quantikine ELISA (R&D Systems, Wiesbaden, Germany)
Intra-assay CV	3.3	2.0
Inter-assay CV	5.0	3.3
Measurement range (for undiluted samples)	0.125 – 8 ng/ml	1.56 – 50 ng/ml
Comments	All samples were measured at 1:10 dilution. All samples yielded values above the lower limit of detection. Samples exceeding the upper limit of detection were measured at 1:20 dilution.	All samples were measured at 1:20 dilution and yielded values within the measurement range.

sE-selectin, soluble E-selectin; sICAM-1, soluble intercellular adhesion molecule-1.

SUPPLEMENTARY DATA

Supplementary Table S1. Description of biospecimen handling and laboratory analyses (contd.).

	GAD	ICA
Biospecimen type	Serum from whole blood with clot activator	Serum from whole blood with clot activator
Storage duration until analysis	0-14 d	0-14 d
Storage temperature	4° C	4° C
Freeze-thaw cycles before analysis	0	0
Assay	Radioimmuno assay (CentAK anti-GAD65, Medipan GmbH, Berlin, Germany)	Indirect immunofluorescence (on human pancreatic tissue)
Intra-assay CV	< 10%	n/a
Inter-assay CV	< 10%	n/a
Measurement range (for undiluted samples)	0.1 – 120 U/ml	n/a
Comments	Classified as negative if GAD<0.9 U/ml.	Antibody titers are determined from serial dilutions of the serum samples and expressed as JDF units. Classified as negative if ICA=0 JDF units.

GAD, glutamic acid decarboxylase autoantibodies; ICA, islet cell autoantibodies; n/a, not applicable.

SUPPLEMENTARY DATA

Supplementary Table S2. Patient numbers, R^2 values, and *P* values from the F-statistic for associations between changes of the markers of low-grade inflammation and changes of glycemic control, insulin secretion, and glucose disappearance rate within the first two years after diabetes diagnosis in patients with type 2 diabetes.

Variable/model	hsCRP			IL-6			IL-18			sE-selectin			sICAM-1		
	N	R^2	F (*P*)	N	R^2	F (*P*)	N	R^2	F (*P*)	N	R^2	F (*P*)	N	R^2	F (*P*)
Glycemic control															
HbA_{1c}															
Model 1	74	0.30	<0.001	93	0.26	<0.001	94	0.26	<0.001	93	0.36	<0.001	93	0.39	<0.001
Model 2	74	0.33	0.006	93	0.31	0.002	94	0.30	0.002	93	0.40	<0.001	93	0.41	<0.001
Indices of insulin secretion															
C-peptide secretion capacity															
Model 1	59	0.26	0.006	75	0.18	0.017	76	0.13	0.077	75	0.19	0.013	75	0.16	0.034
Model 2	59	0.44	0.002	75	0.38	0.001	76	0.37	0.002	75	0.39	0.001	75	0.37	0.002
ACPRG															
Model 1	59	0.59	<0.001	75	0.66	<0.001	76	0.63	<0.001	75	0.62	<0.001	75	0.65	<0.001
Model 2	59	0.61	<0.001	75	0.67	<0.001	76	0.65	<0.001	75	0.64	<0.001	75	0.67	<0.001
$iAUC_{CP}$															
Model 1	59	0.39	<0.001	75	0.47	<0.001	76	0.43	<0.001	75	0.43	<0.001	75	0.44	<0.001
Model 2	59	0.41	0.005	75	0.50	<0.001	76	0.45	<0.001	75	0.45	<0.001	75	0.46	<0.001
Pre-hepatic iBCF															
Model 1	56	0.44	<0.001	71	0.49	<0.001	72	0.46	<0.001	71	0.48	<0.001	71	0.46	<0.001
Model 2	56	0.49	0.001	71	0.52	<0.001	72	0.49	<0.001	71	0.52	<0.001	71	0.49	<0.001
Measure of intravenous glucose tolerance															
Glucose disappearance rate															
Model 1	59	0.10	0.350	74	0.12	0.128	75	0.10	0.206	74	0.09	0.254	74	0.10	0.209
Model 2	59	0.22	0.313	74	0.20	0.263	75	0.20	0.268	74	0.19	0.317	74	0.19	0.284

The table gives patient numbers (N), R^2 values, and *P* values from F-statistic. Model 1 adjusted for the independent variable at baseline, concentration of the marker of low-grade inflammation at baseline, age at baseline, and sex and model 2 additionally adjusted for BMI at baseline, change of BMI, change of the type of glucose-lowering medication, smoking status at baseline, and change of smoking status.

C-peptide secretion capacity, ACPRG, $iAUC_{CP}$, pre-hepatic iBCF, hsCRP, IL-6, IL-18, sE-selectin, and sICAM-1 entered the models as ln-transformed variables. C-peptide secretion capacity as ratio of C-peptide 6min/C-peptide 0min from glucagon stimulation test.

ACPRG, acute C-peptide glucose-dependent response; hsCRP, high-sensitivity C-reactive protein; $iAUC_{CP}$, glucose-stimulated total incremental area under the curve for C-peptide; iBCF, incremental pre-hepatic beta-cell function; IL, interleukin; sE-selectin, soluble E-selectin (sE-selectin); sICAM-1, soluble intercellular adhesion molecule-1.

SUPPLEMENTARY DATA

Supplementary Table S3. Patient numbers, R^2 values, and *P* values from the F-statistic for associations between changes of the markers of low-grade inflammation and changes of glycemic control, insulin secretion, and glucose disappearance rate within the first two years after diabetes diagnosis in patients with type 1 diabetes.

Variable/model	hsCRP			IL-6			IL-18			sE-selectin			sICAM-1		
	N	R^2	F (*P*)	N	R^2	F (*P*)	N	R^2	F (*P*)	N	R^2	F (*P*)	N	R^2	F (*P*)
Glycemic control															
HbA_{1c}															
Model 1	38	0.24	0.110	42	0.42	0.001	42	0.34	0.009	42	0.24	0.065	42	0.20	0.136
Model 2	38	0.48	0.080	42	0.52	0.018	42	0.49	0.030	42	0.38	0.186	42	0.36	0.253
Indices of insulin secretion															
C-peptide secretion capacity															
Model 1	26	0.36	0.089	30	0.38	0.031	30	0.37	0.037	30	0.47	0.006	30	0.38	0.035
Model 2	26	0.54	0.236	30	0.62	0.031	30	0.55	0.092	30	0.59	0.048	30	0.59	0.049
ACPRG															
Model 1	26	0.71	<0.001	30	0.72	<0.001	30	0.72	<0.001	30	0.72	<0.001	30	0.75	<0.001
Model 2	26	0.82	0.002	30	0.81	<0.001	30	0.80	<0.001	30	0.81	<0.001	30	0.80	<0.001
$iAUC_{CP}$															
Model 1	26	0.69	<0.001	30	0.71	<0.001	30	0.69	<0.001	30	0.69	<0.001	30	0.71	<0.001
Model 2	26	0.81	0.002	30	0.78	<0.001	30	0.74	0.002	30	0.76	0.001	30	0.76	0.001
Pre-hepatic iBCF															
Model 1	23	0.72	<0.001	27	0.72	<0.001	27	0.70	<0.001	27	0.71	<0.001	27	0.72	<0.001
Model 2	23	0.79	0.019	27	0.76	0.005	27	0.73	0.011	27	0.78	0.003	27	0.76	0.005
Measure of intravenous glucose tolerance															
Glucose disappearance rate															
Model 1	31	0.40	0.020	35	0.38	0.014	35	0.37	0.017	35	0.39	0.011	35	0.35	0.022
Model 2	31	0.65	0.026	35	0.67	0.004	35	0.65	0.006	35	0.63	0.009	35	0.63	0.011

The table gives patient numbers (N), R^2 values, and *P* values from F-statistic. Model 1 adjusted for the independent variable at baseline, concentration of the marker of low-grade inflammation at baseline, age at baseline, and sex and model 2 additionally adjusted for BMI at baseline, change of BMI, change of the type of glucose-lowering medication, smoking status at baseline, and change of smoking status.

C-peptide secretion capacity, ACPRG, $iAUC_{CP}$, pre-hepatic iBCF, hsCRP, IL-6, IL-18, sE-selectin, and sICAM-1 entered the models as ln-transformed variables. C-peptide secretion capacity as ratio of C-peptide 6min/C-peptide 0min from glucagon stimulation test.

ACPRG, acute C-peptide glucose-dependent response; hsCRP, high-sensitivity C-reactive protein; $iAUC_{CP}$, glucose-stimulated total incremental area under the curve for C-peptide; iBCF, incremental pre-hepatic beta-cell function; IL, interleukin; sE-selectin, soluble E-selectin (sE-selectin); sICAM-1, soluble intercellular adhesion

SUPPLEMENTARY DATA

Supplementary Table S4. Power calculations for the given data for associations between changes of the markers of low-grade inflammation and changes of glycemic control, insulin secretion, and glucose disappearance rate within the first two years after diabetes diagnosis in patients with type 2 diabetes.

Variable /model	hsCRP		Il-6		IL-18		sE-selectin		sICAM-1	
	N	Power	N	Power	N	Power	N	Power	N	Power
Glycemic control HbA_{1c}										
Model 1	51	93.6%	237	40.5%	276	35.8%	63	93.4%	39	99.5%
Model 2	59	89.5%	447	22.8%	372	26.9%	66	92.8%	51	98.1%
Indices of insulin secretion C-peptide secretion capacity										
Model 1	76	68.6%	154	48.1%	4589	<10%	125	57.1%	340	24.6%
Model 2	292	21.1%	1216	<10%	9013	<10%	275	28.1%	1138	10.2%
ACPRG										
Model 1	2846	<10%	4755	<10%	3961	<10%	>10,000	<10%	182	41.8%
Model 2	8751	<10%	>10,000	<10%	4873	<10%	>10,000	<10%	135	52.1%
$iAUC_{CP}$										
Model 1	1320	<10%	182	41.9%	851	12.6%	697	14.3%	317	26.1%
Model 2	2177	<10%	135	52.0%	719	13.5%	394	20.8%	311	25.2%
Pre-hepatic iBCF										
Model 1	225	26.6%	364	22.1%	376	21.8%	115	58.1%	238	31.6%
Model 2	302	19.5%	220	32.2%	251	29.2%	97	65.2%	228	31.3%
Measure of intravenous glucose tolerance Glucose disappearance rate										
Model 1	7102	<10%	>10,000	<10%	2081	<10%	>10,000	<10%	861	12.3%
Model 2	917	<10%	9942	<10%	>10,000	<10%	>10,000	<10%	1113	10.2%

The table gives patient numbers (N) to detect significant differences based on observed partial correlations for a power of 80% and calculated power of observed partial correlations based on patient numbers as described in Table S2. Model 1 adjusted for the independent variable at baseline, concentration of the marker of low-grade inflammation at baseline, age at baseline, and sex and model 2 additionally adjusted for BMI at baseline, change of BMI, change of the type of glucose-lowering medication, smoking status at baseline, and change of smoking status.

C-peptide secretion capacity, ACPRG, $iAUC_{CP}$, pre-hepatic iBCF, hsCRP, IL-6, IL-18, sE-selectin, and sICAM-1 entered the models as ln-transformed variables. C-peptide secretion capacity as ratio of C-peptide 6min/C-peptide 0min from glucagon stimulation test.

ACPRG, acute C-peptide glucose-dependent response; hsCRP, high-sensitivity C-reactive protein; $iAUC_{CP}$, glucose-stimulated total incremental area under the curve for C-peptide; iBCF, incremental pre-hepatic beta-cell function; IL, interleukin; sE-selectin, soluble E-selectin (sE-selectin); sICAM-1, soluble intercellular adhesion molecule-1.

SUPPLEMENTARY DATA

Supplementary Table S5. Power calculations for the given data for associations between changes of the markers of low-grade inflammation and changes of glycemic control, insulin secretion, and glucose disappearance rate within the first two years after diabetes diagnosis in patients with type 1 diabetes.

Variable/ model	hsCRP		IL-6		IL-18		sE-selectin		sICAM-1	
	N	Power	N	Power	N	Power	N	Power	N	Power
Glycemic control HbA_{1c}										
Model 1	226	18.6%	435	12.7%	37	86.4%	3503	<10%	4921	<10%
Model 2	188	19.1%	>10,000	<10%	36	88.1%	361	13.1%	1284	<10%
Indices of insulin secretion C-peptide secretion capacity										
Model 1	348	10.2%	4441	<10%	2910	<10%	52	52.5%	887	<10%
Model 2	340	<10%	1091	<10%	7135	<10%	86	28.8%	1073	<10%
ACPRG										
Model 1	878	<10%	184	17.5%	212	15.7%	202	16.3%	59	47.0%
Model 2	1555	<10%	113	22.2%	403	<10%	171	15.8%	345	10.0%
$iAUC_{CP}$										
Model 1	1178	<10%	197	16.5%	402	10.4%	755	<10%	88	32.5%
Model 2	159	14.1%	83	29.8%	>10,000	<10%	132	19.5%	>10,000	<10%
Pre-hepatic iBCF										
Model 1	148	15.8%	9963	<10%	1566	<10%	497	<10%	117	22.7%
Model 2	59	28.2%	574	<10%	>10,000	<10%	105	20.6%	>10,000	<10%
Measure of intravenous glucose tolerance Glucose disappearance rate										
Model 1	148	21.5%	138	25.7%	208	18.3%	112	30.8%	>10,000	<10%
Model 2	6367	<10%	63	47.5%	82	36.7%	142	22.0%	1910	<10%

The table gives patient numbers (N) to detect significant differences based on observed partial correlations for a power of 80% and calculated power of observed partial correlations based on patient numbers as described in Table S3. Model 1 adjusted for the independent variable at baseline, concentration of the marker of low-grade inflammation at baseline, age at baseline, and sex and model 2 additionally adjusted for BMI at baseline, change of BMI, change of the type of glucose-lowering medication, smoking status at baseline, and change of smoking status.

C-peptide secretion capacity, ACPRG, $iAUC_{CP}$, pre-hepatic iBCF, hsCRP, IL-6, IL-18, sE-selectin, and sICAM-1 entered the models as ln-transformed variables. C-peptide secretion capacity as ratio of C-peptide 6min/C-peptide 0min from glucagon stimulation test.

ACPRG, acute C-peptide glucose-dependent response; hsCRP, high-sensitivity C-reactive protein; $iAUC_{CP}$, glucose-stimulated total incremental area under the curve for C-peptide; iBCF, incremental pre-hepatic beta-cell function; IL, interleukin; sE-selectin, soluble E-selectin (sE-selectin); sICAM-1, soluble intercellular adhesion molecule-1.

SUPPLEMENTARY DATA

Supplementary Table S6. Power calculations for defined clinically relevant changes for associations between changes of the markers of low-grade inflammation and changes of glycemic control, insulin secretion, and glucose disappearance rate within the first two years after diabetes diagnosis in patients with type 2 diabetes.

Variable /model	hsCRP		Il-6		IL-18		sE-selectin		sICAM-1	
	N	Power	N	Power	N	Power	N	Power	N	Power
Glycemic control										
HbA_{1c}*										
Model 1	42	97.1%	68	91.3%	163	55.6%	193	48.2%	483	22.3%
Model 2	52	94.0%	77	87.8%	178	50.8%	203	44.9%	517	20.3%
Indices of insulin secretion										
C-peptide secretion capacity†										
Model 1	35	96.8%	77	79.3%	168	45.3%	278	29.1%	573	16.4%
Model 2	33	98.6%	71	82.9%	142	50.7%	234	32.3%	480	17.8%
ACPRG†										
Model 1	62	78.3%	98	68.0%	225	35.3%	371	22.9%	783	13.2%
Model 2	73	69.3%	118	58.3%	240	32.0%	413	20.0%	849	12.0%
$iAUC_{CP}$†										
Model 1	225	28.0%	461	19.3%	1042	11.2%	1666	<10%	3723	<10%
Model 2	255	23.6%	531	16.5%	1098	10.5%	1881	<10%	4093	<10%
Pre-hepatic iBCF†										
Model 1	206	28.7%	393	20.8%	884	11.9%	1713	<10%	3148	<10%
Model 2	211	26.3%	440	18.1%	926	11.1%	1835	<10%	3345	<10%
Measure of intravenous glucose tolerance										
Glucose disappearance rate‡										
Model 1	54	83.9%	87	73.0%	199	38.7%	257	30.7%	583	16.0%
Model 2	60	79.8%	95	68.2%	198	37.4%	260	29.0%	627	14.5%

The table gives patient numbers (N) and the calculated power for defined clinically relevant changes. Change of *HbA_{1c} by 0.5%, of †C-peptide secretion capacity, ACPRG, $iAUC_{CP}$, and iBCF by 10%, and of ‡glucose disappearance rate by 0.1%/min with a doubling of the ratio of the independent variable. Model 1 adjusted for the independent variable at baseline, concentration of the marker of low-grade inflammation at baseline, age at baseline, and sex and model 2 additionally adjusted for BMI at baseline, change of BMI, change of the type of glucose-lowering medication, smoking status at baseline, and change of smoking status. C-peptide secretion capacity, ACPRG, $iAUC_{CP}$, pre-hepatic iBCF, hsCRP, IL-6, IL-18, sE-selectin, and sICAM-1 entered the models as ln-transformed variables. C-peptide secretion capacity as ratio of C-peptide 6min/C-peptide 0min from glucagon stimulation test.

ACPRG, acute C-peptide glucose-dependent response; hsCRP, high-sensitivity C-reactive protein; $iAUC_{CP}$, glucose-stimulated total incremental area under the curve for C-peptide; iBCF, incremental pre-hepatic beta-cell function; IL, interleukin; sE-selectin, soluble E-selectin (sE-selectin); sICAM-1, soluble intercellular adhesion

SUPPLEMENTARY DATA

Supplementary Table S7. Power calculations for defined clinically relevant changes for associations between changes of the markers of low-grade inflammation and changes of glycemic control, insulin secretion, and glucose disappearance rate within the first two years after diabetes diagnosis in patients with type 1 diabetes.

Variable/ model	hsCRP		IL-6		IL-18		sE-selectin		sICAM-1	
	N	Power	N	Power	N	Power	N	Power	N	Power
Glycemic control HbA_{1c}*										
Model 1	63	56.0%	68	57.5%	186	23.9%	455	12.3%	937	<10%
Model 2	75	44.2%	80	46.5%	173	22.9%	548	10.2%	939	<10%
Indices of insulin secretion C-peptide secretion capacity†										
Model 1	88	28.0%	157	19.7%	194	16.7%	808	<10%	1551	<10%
Model 2	87	23.3%	172	15.8%	180	15.2%	815	<10%	1975	<10%
ACPRG†										
Model 1	549	<10%	1065	<10%	1249	<10%	5272	<10%	9812	<10%
Model 2	451	<10%	1242	<10%	1057	<10%	5215	<10%	>10,000	<10%
$iAUC_{CP}$†										
Model 1	1447	<10%	2865	<10%	3238	<10%	>10,000	<10%	>10,000	<10%
Model 2	1224	<10%	3603	<10%	3455	<10%	>10,000	<10%	>10,000	<10%
Pre-hepatic iBCF†										
Model 1	1658	<10%	2533	<10%	3477	<10%	>10,000	<10%	>10,000	<10%
Model 2	1977	<10%	4371	<10%	3844	<10%	>10,000	<10%	>10,000	<10%
Measure of intravenous glucose tolerance Glucose disappearance rate‡										
Model 1	79	37.3%	119	29.2%	267	15.2%	609	<10%	1217	<10%
Model 2	90	28.8%	112	27.3%	213	15.9%	521	<10%	896	<10%

The table gives patient numbers (N) and the calculated power for defined clinically relevant changes. Change of *HbA_{1c} by 0.5%, of †C-peptide secretion capacity, ACPRG, $iAUC_{CP}$, and iBCF by 10%, and of ‡glucose disappearance rate by 0.1%/min with a doubling of the ratio of the independent variable. Model 1 adjusted for the independent variable at baseline, concentration of the marker of low-grade inflammation at baseline, age at baseline, and sex and model 2 additionally adjusted for BMI at baseline, change of BMI, change of the type of glucose-lowering medication, smoking status at baseline, and change of smoking status. C-peptide secretion capacity, ACPRG, $iAUC_{CP}$, pre-hepatic iBCF, hsCRP, IL-6, IL-18, sE-selectin, and sICAM-1 entered the models as ln-transformed variables. C-peptide secretion capacity as ratio of C-peptide 6min/C-peptide 0min from glucagon stimulation test.

ACPRG, acute C-peptide glucose-dependent response; hsCRP, high-sensitivity C-reactive protein; $iAUC_{CP}$, glucose-stimulated total incremental area under the curve for C-peptide; iBCF, incremental pre-hepatic beta-cell function; IL, interleukin; sE-selectin, soluble E-selectin (sE-selectin); sICAM-1, soluble intercellular adhesion molecule-1.

SUPPLEMENTARY DATA

Supplementary Table S8. Associations between changes of the markers of low-grade inflammation and changes of glycemic control, insulin secretion, and glucose disappearance rate within the first two years after diabetes diagnosis in patients with type 2 without glucose-lowering medication.

Variable/model	hsCRP		IL-6		IL-18		sE-selectin		sICAM-1	
	β (95% CI)	*P*	β (95% CI)	*P*	β (95% CI)	*P*	β (95% CI)	*P*	β (95% CI)	*P*
Glycemic control A1c*										
Model 1	**0.52 (0.17; 0.87)**	**0.005**	**0.47 (0.06; 0.88)**	**0.027**	0.25 (-0.50; 0.99)	0.504	0.32 (-0.27; 0.91)	0.276	**1.37 (0.34; 2.39)**	**0.011**
Model 2	**0.59 (0.20; 0.99)**	**0.005**	**0.48 (0.04; 0.92)**	**0.035**	0.27 (-0.55; 1.08)	0.510	0.55 (-0.13; 1.22)	0.108	**1.57 (0.37; 2.76)**	**0.012**
Measures of insulin secretion C-peptide secretion capacity†										
Model 1	-2.86 (-9.72; 4.51)	0.420	-0.14 (-9.97; 10.75)	0.977	-8.39 (-20.05; 4.98)	0.199	-8.22 (-19.12; 4.16)	0.176	-8.40 (-25.7; 12.91)	0.398
Model 2	0.07 (-7.01; 7.70)	0.983	1.97 (-7.91; 12.91)	0.697	-10.07 (-20.41; 1.60)	0.085	-4.06 (-16.21; 9.87)	0.535	-10.18 (-27.24; 10.88)	0.304
ACPRG†										
Model 1	-5.08 (-13.6; 4.28)	0.264	7.94 (-5.15; 22.83)	0.237	2.10 (-15.27; 23.03)	0.821	2.40 (-13.27; 20.91)	0.772	-10.79 (-32.47; 17.85)	0.409
Model 2	-6.30 (-16.09; 4.63)	0.233	12.58 (-1.95; 29.26)	0.090	2.48 (-16.11; 25.18)	0.803	5.48 (-12.65; 27.37)	0.566	-12.36 (-36.70; 21.33)	0.412
$iAUC_{CP}$†										
Model 1	-14.61 (-29.37; 3.24)	0.099	16.55 (-13.11; 56.33)	0.295	11.30 (-25.23; 65.68)	0.587	1.46 (-28.47; 43.92)	0.933	-26.86 (-60.48; 35.37)	0.308
Model 2	-10.75 (-27.9; 10.48)	0.279	20.21 (-12.25; 64.68)	0.240	17.29 (-22.02; 76.44)	0.429	5.02 (-28.80; 54.90)	0.798	-35.94 (-67.29; 25.46)	0.185
Pre-hepatic iBCF†										
Model 1	**-16.09 (-27.74; -2.55)**	**0.024**	9.77 (-15.91; 43.28)	0.479	2.14 (-30.58; 50.27)	0.911	-22.75 (-45.96; 10.42)	0.150	-34.52 (-61.58; 11.60)	0.115
Model 2	**-14.35 (-26.31; -0.46)**	**0.044**	6.39 (-20.44; 42.27)	0.664	0.04 (-35.04; 54.06)	0.998	-23.33 (-47.56; 12.09)	0.161	-50.78 (-71.15; -16.02)	**0.012**
Measure of intravenous glucose tolerance Glucose disappearance rate*										
Model 1	-0.03 (-0.12; 0.06)	0.535	0.09 (-0.03; 0.21)	0.124	0.02 (-0.18; 0.22)	0.825	0.03 (-0.14; 0.19)	0.742	-0.01 (-0.28; 0.26)	0.923
Model 2	-0.02 (-0.12; 0.08)	0.743	0.09 (-0.03; 0.22)	0.131	-0.04 (-0.26; 0.18)	0.698	-0.01 (-0.20; 0.18)	0.898	0.05 (-0.26; 0.37)	0.728

The table gives regression coefficients (β), 95% confidence intervals (95% CI), and *P* values from linear regression analyses with model 1 adjusted for the dependent variable at baseline, concentration of the marker of low-grade inflammation at baseline, age at baseline, sex, and diabetes type, and model 2 additionally adjusted for BMI at baseline, change of BMI, smoking status at baseline, and change of smoking status. C-peptide secretion capacity, ACPRG, $iAUC_{CP}$, pre-hepatic iBCF, hsCRP, IL-6, IL-18, sE-selectin, and sICAM-1 entered the models as ln-transformed variables. *Bold* indicates significant associations ($P<0.05$). C-peptide secretion capacity as ratio of C-peptide 6min/C-peptide 0min from glucagon stimulation test.

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ACPRG, acute C-peptide glucose-dependent response; hsCRP, high-sensitivity C-reactive protein; $iAUC_{CP}$, glucose-stimulated total incremental area under the curve for C-peptide; iBCF, incremental pre-hepatic beta-cell function; IL, interleukin; sE-selectin, soluble E-selectin (sE-selectin); sICAM-1, soluble intercellular adhesion molecule-1.

Regression coefficients should be interpreted as follows: *A doubling of the ratio of hsCRP, IL-6, IL-18, sE-selectin, and sICAM-1 within the first two years after diabetes diagnosis associates with an absolute change of HbA_{1c} and glucose disappearance rate within the first two years by β. †A doubling of the ratio of 2year/baseline values of hsCRP, IL-6, IL-18, sE-selectin, and sICAM-1 associates with a %-change of C-peptide secretion capacity, ACPRG, $iAUC_{CP}$, and iBCF within the first two years by β.

SUPPLEMENTARY DATA

Supplementary Table S9. Patient numbers, R^2 values, and *P* values from the F-statistic for associations between changes of the markers of low-grade inflammation and changes of glycemic control, insulin secretion, and glucose disappearance rate within the first two years after diabetes diagnosis in patients with type 2 diabetes without glucose-lowering medication.

Variable/model	hsCRP			IL-6			IL-18			sE-selectin			sICAM-1		
	N	R^2	F(*P*)	N	R^2	F(*P*)	N	R^2	F(*P*)	N	R^2	F(*P*)	N	R^2	F(*P*)
Glycemic control A1c*															
Model 1	35	0.57	<0.001	42	0.51	<0.001	42	0.45	<0.001	42	0.46	<0.001	42	0.53	<0.001
Model 2	35	0.59	0.003	42	0.54	0.001	42	0.47	0.009	42	0.52	0.003	42	0.55	<0.001
Measures of insulin secretion C-peptide secretion capacity†															
Model 1	30	0.29	0.114	36	0.36	0.016	36	0.40	0.007	36	0.40	0.007	36	0.37	0.012
Model 2	30	0.51	0.059	36	0.53	0.008	36	0.61	0.001	36	0.54	0.007	36	0.56	0.005
ACPRG†															
Model 1	30	0.71	<0.001	36	0.75	<0.001	36	0.73	<0.001	36	0.73	<0.001	36	0.73	<0.001
Model 2	30	0.73	<0.001	36	0.78	<0.001	36	0.75	<0.001	36	0.75	<0.001	36	0.75	<0.001
$iAUC_{CP}$†															
Model 1	30	0.57	<0.001	36	0.53	<0.001	36	0.55	<0.001	36	0.55	<0.001	36	0.54	<0.001
Model 2	30	0.63	<0.001	36	0.59	0.002	36	0.62	0.001	36	0.62	0.001	36	0.62	0.001
Pre-hepatic iBCF†															
Model 1	28	0.72	<0.001	33	0.59	<0.001	33	0.57	<0.001	33	0.61	<0.001	33	0.61	<0.001
Model 2	28	0.82	<0.001	33	0.64	0.002	33	0.63	0.002	33	0.66	<0.001	33	0.73	<0.001
Measure of intravenous glucose tolerance Glucose disappearance rate*															
Model 1	30	0.27	0.167	35	0.35	0.027	35	0.24	0.143	35	0.24	0.136	35	0.29	0.065
Model 2	30	0.37	0.299	35	0.46	0.044	35	0.35	0.195	35	0.35	0.200	35	0.40	0.104

The table gives patient numbers (N), R^2 values, and *P* values from F-statistic. Model 1 adjusted for the independent variable at baseline, concentration of the marker of low-grade inflammation at baseline, age at baseline, and sex and model 2 additionally adjusted for BMI at baseline, change of BMI, smoking status at baseline, and change of smoking status.

C-peptide secretion capacity, ACPRG, $iAUC_{CP}$, pre-hepatic iBCF, hsCRP, IL-6, IL-18, sE-selectin, and sICAM-1 entered the models as ln-transformed variables. C-peptide secretion capacity as ratio of C-peptide 6min/C-peptide 0min from glucagon stimulation test.

ACPRG, acute C-peptide glucose-dependent response; hsCRP, high-sensitivity C-reactive protein; $iAUC_{CP}$, glucose-stimulated total incremental area under the curve for C-peptide; iBCF, incremental pre-hepatic beta-cell function; IL, interleukin; sE-selectin, soluble E-selectin (sE-selectin); sICAM-1, soluble intercellular adhesion molecule-1.

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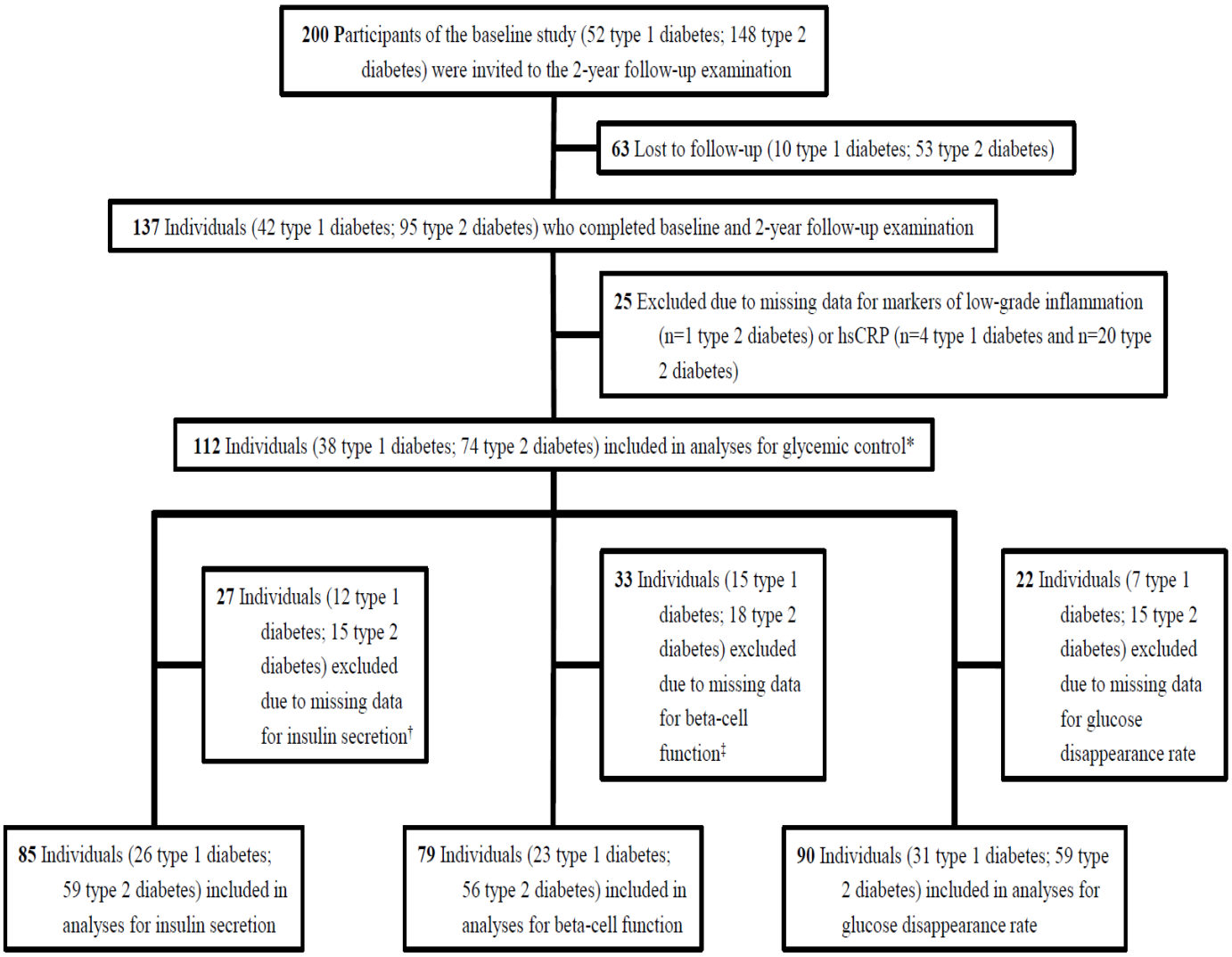
Supplementary Table S10. Characteristics of participants vs. drop-outs.

	Type 2 diabetes			Type 1 diabetes		
	Participants	Drop-outs	*P**	Participants	Drop-outs	*P**
N	95	53	0.115	42	10	1.000
Age [years]	54±10	49±11	**0.033**	35±12	36±10	0.710
Sex (males/females)	68/27 (72/28%)	31/22 (58/42%)	0.145	23/19 (55/45%)	5/5 (50/50%)	1.000
BMI [kg/m^2]	31.5±5.8	31.5±5.7	0.774	24.8±4.0	26.6±6.6	0.456
HbA_{1c} [% (mmol/mol)]	6.46±1.01 (47±11)	7.01±1.73 (53±19)	0.065	7.08±1.58 (54±17)	7.98±3.17 (64±35)	0.561
Duration since diagnosis of diabetes [days]	165±110	123±91	**0.026**	177±109	155±112	0.546

Data are given as n, % or mean±SD.
*Fisher's exact test for categorical variables and Wilcoxon-signed ranked test for continuous variables to test for differences between participants and drop-outs. *Bold* indicates significant differences ($P<0.05$).
BMI, body mass index.

SUPPLEMENTARY DATA

Supplementary Figure 1. Flow diagram showing the number of patients included in the analyses for hsCRP from those enrolled in the German Diabetes Study.



*Hb_{A1c}. †C-peptide secretion from glucagon stimulation test, acute C-peptide glucose-dependent response (ACPRG), and glucose-stimulated total incremental area under the curve for C-peptide ($iAUC_{CP}$). ‡Incremental pre-hepatic beta-cell function (iBCF). Persons who were lost to follow-up were deceased, seriously ill, not to be contacted, no longer interested in or lacking time for study participation, or declined without giving a reason.

SUPPLEMENTARY DATA

Supplementary Reference List

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