J. Clin. Chem. Clin. Biochem.
Vol. 22, 1984, pp. 591–596

The Relationship of Lipoprotein (a) (Lp(a)) to Risk Factors of Coronary Heart Disease:

Initial results of the prospective epidemiological study on company employees in Westfalia

By *H. Schriewer, G. Assmann, M. Sandkamp*

Institut für Klinische Chemie und Laboratoriumsmedizin (Zentrallaboratorium), Medizinische Einrichtungen der Westfälischen Wilhelms-Universität, Münster and

H. Schulte

Institut für Arteriosklerosеforschung, Westfälische Wilhelms-Universität, Münster

(Received March 12/June 5, 1984)

Summary: Lp(a) concentrations were determined in 987 male and 477 female company employees in Westfalia, in the age range 17–70 years. These values were then related to age and to the following risk factors: obesity, smoking, hypertension, hypertriglyceridaemia, hypercholesterolaemia, hyperbetalipoproteinaemia, hypoalphalipoproteinaemia, hyperglycaemia and hyperuricaemia.

The Lp(a) values showed a similar markedly skewed distribution for both men and women. The median for men was 0.039 g/l, for women 0.050 g/l. In both sexes only about 25% of all Lp(a) values were above 0.10 g/l. Raised Lp(a) values (>0.30 g/l) were found in 6.5% of males and in 6.1% of females.

A significantly higher frequency of raised Lp(a) values (>0.30 g/l) was found in: post-menopausal women (11.3% as against 4.1%, $p < 0.01$); females with hypercholesterolaemia (19.0% when cholesterol values were ≥6.73 mmol/l, 10.8 % when cholesterol values were between 5.70–6.72 mmol/l, 3.0% when cholesterol values were <5.70 mmol/l, $p < 0.001$); and females with hyperbetalipoproteinaemia (22.6% when LDL cholesterol values were ≥4.92 mmol/l, 5.0% when LDL cholesterol values were <4.92 mmol/l, $p < 0.001$).

12.0% of men with hypoalphalipoproteinaemia (HDL cholesterol values <0.907 mmol/l) had Lp(a) values >0.30 g/l, as against 5.5% of men with HDL cholesterol values ≥0.907 mmol/l ($p < 0.01$).

This percentage rate increased to 16.9% when hypertriglyceridaemia (≥2.28 mmol/l triglycerides) was also present. All other risk factors which were examined and their combinations had no significant influence on the prevalence of raised Lp(a) concentrations.

Beziehung von Lipoprotein (a) (Lp(a)) zu Risikofaktoren der koronaren Herzkrankheit: Erste Ergebnisse der prospektiven epidemiologischen Studie bei Betriebsangehörigen in Westfalen

Zusammenfassung: Bei 987 männlichen und 477 weiblichen Betriebsangehörigen in Westfalen im Alter von 17–70 Jahren wurden die Lp(a)-Konzentrationen im Serum bestimmt und zum Alter und zu folgenden Risikofaktoren in Beziehung gesetzt: Übergewicht, Rauchen, Hypertonie, Hypertriglyceridämie, Hypercholesterinämie, Hyperbetalipoproteinämie, Hypoalphalipoproteinämie, Hyperglykämie und Hyperurikämie.

Die Lp(a) Werte wiesen bei beiden Geschlechtern annähernd die gleiche auffällig schiefe Verteilung auf. Der Median betrug bei Männern 0,039 g/l, bei Frauen 0,050 g/l. Bei beiden Geschlechtern lagen nur etwa 25% aller Lp(a)-Werte über 0,10 g/l. Erhöhte Lp(a)-Werte (>0,30 g/l) wiesen 6,5% der Männer und 6,1% der Frauen auf.

Signifikant größere relative Häufigkeiten von erhöhten Lp(a)-Konzentrationen (>0,30 g/l) traten auf: bei Frauen nach Eintritt der Menopause (11,3% gegenüber 4,1%, $p < 0,01$), bei weiblichen Probanden mit Hypercholesterinämie (19,0% bei Cholesterinwerten ≥6,73 mmol/l, 10,8% bei Cholesterinwerten von 5,70–6,72 mmol/l, 3,0% bei Cholesterinwerten <5,70 mmol/l, $p < 0,001$), und mit Hyperbetalipoproteinämie (22,6% bei LDL-Cholesterinwerten ≥4,92 mmol/l, 5,0% bei LDL-Cholesterinwerten <4,92 mmol/l, $p < 0,001$).

Bei Männern mit Hypoalphalipoproteinämie (HDL-Cholesterinwerte <0,907 mmol/l) traten in 12,0% Lp(a)-Werte größer als 0,30 g/l auf, gegenüber 5,5% bei Probanden mit HDL-Cholesterinwerten ≥0,907 mmol/l, $p < 0,01$). Dieser Prozentsatz stieg auf 16,9% an, falls gleichzeitig eine Hypertriglyceridämie vorlag (Triglyceride ≥2,28 mmol/l). Alle anderen untersuchten Risikofaktoren und deren Kombinationen hatten keinen signifikanten Einfluß auf die Prävalenz erhöhter Lp(a)-Konzentrationen.

Introduction

Lipoprotein (a) (Lp(a)) is a cholesterol-rich lipoprotein in blood serum with electrophoretic pre-β-mobility (1) and a lipid composition similar to low density lipoproteins (LDL) (2). Like LDL, Lp(a) contains mainly apolipoprotein B (62%), but also Lp(a) apolipoprotein (20%) and albumin (15%) (3). Unlike LDL, Lp(a) floats in a higher density range (1.055–1.110 kg/l) (4) and has a higher proportion of carbohydrate (3). Lp(a) is present in almost all individuals, although the concentrations can vary quite considerably (5).

Various projects agree in their findings that individuals with raised Lp(a) values run a higher risk of developing coronary heart disease prematurely (6–8). Lp(a) does not correlate significantly with other risk factors such as age, sex, cholesterol, triglycerides (1, 8, 9) or cigarette smoking (10). Results of epidemiological studies on the correlation of Lp(a) values and premature development of coronary heart disease have not been available until now.

This present study reports the first results of our epidemiological study on the distribution of Lp(a) values in company employees in Westfalia, and the correlation of Lp(a) values to risk factors for coronary heart disease in these subjects.

Materials and Methods

Sample material

As test material we used fresh serum from the test series "Prospective epidemiological study of company employees in Westfalia" (11).

Methods

Analyses of cholesterol, triglycerides, glucose and uric acid were performed with the SMAC Analyser (Technicon GmbH, Bad Vilbel, FRG) as described elsewhere (11).

Lipoprotein (a) assay

For the determination of lipoprotein (a) (Lp(a)) in blood serum, one dimensional *Laurell* immunelectrophoresis was used (12). As antibody we used Antihuman Lp(a) from sheep (Immuno Comp., D-6900 Heidelberg, order no. 4845005).

As standard reference Human Lp(a) (Immuno Comp. D-6900 Heidelberg, order no. 4395005) was used.

Analysis of HDL components

HDL cholesterol was enzymatically analysed using the CHOD-PAP method (Boehringer Mannheim, test combination no. 187313), as described elsewhere (13). Determination of HDL phosphatidyl choline was carried out as enzymatic colour test using the centrifugal analyser Cobas Bio (Hoffmann La Roche). This method is described in detail elsewhere (14).

Analysis of LDL components

LDL cholesterol and LDL apolipoprotein B were determined following selective precipitation of VLDL with phosphotungstic acid/$MgCl_2$ as described in detail elsewhere (15).

Statistics

Comparisons of frequencies were done by the χ^2-test. To test whether two distributions are equal, we used the *Mann-Whitney* U-test, and for multiple comparisons the test by *Nemenyi*. We calculated with *Kendall*'s τ instead of *Spearman*'s rank correlation coefficients because of the high number of tied ranks.

The significance level was set at 0.05.

Results

Description of the test group

Lp(a) concentrations in serum were determined in 987 male and 477 female company employees in Westfalia. The average age of the men was 42.1 years (± 10.8 years), of the women 36.4 years (± 13.2 years), age range: 17 to 70 years. The medium *Broca* index for men was 104.0% ± 13.3%, with a range of 72% to 161%, for women 99.0% ± 16.6%, with a range of 69% to 165%; 30.7% of the men were smokers with an average consumption of 18.8

Tab. 1. Distribution parameters of measured values in men (n = 987).
Prospective epidemiological study of company employees in Westfalia.

	Median	Standard deviation	Minimum	Maximum
Age (years)	42.1	10.8	17	70
Broca-Index (%)	104.0	13.3	72	161
Systolic blood pressure (mm Hg)	129	16	95	190
Diastolic blood pressure (mm Hg)	85	10	60	125
Cholesterol (mmol/l)	5.49	1.08	2.18	9.04
Triglycerides (mmol/l)	1.66	1.21	0.25	12.20
HDL Cholesterol (mmol/l)	1.18	0.29	0.57	2.44
LDL Cholesterol (mmol/l)	3.57	1.00	0.41	7.15
HDL Phosphatidyl choline (mmol/l)	1.17	0.23	0.62	2.46
Net Cholesterol (mmol/l)	5.40	1.07	2.06	9.02
LDL Apolipoprotein B (g/l) (n = 300)	0.966	0.253	0.146	2.200
Blood sugar (mmol/l)	5.46	0.88	3.72	7.62
Uric acid (µmol/l)	327	65	107	601
Cigarettes/day (n = 303 smokers)	18.8	9.4	2	50

Tab. 2. Distribution parameters of measured values in women (n = 477).
Prospective epidemiological study of company employees in Westfalia.

	Median	Standard deviation	Minimum	Maximum
Age (years)	36.4	13.2	17	67
Broca-Index (%)	99.1	16.6	69	165
Systolic blood pressure (mm Hg)	124	18	85	230
Diastolic blood pressure (mm Hg)	82	11	50	160
Cholesterol (mmol/l)	5.22	1.12	2.88	11.68
Triglycerides (mmol/l)	1.05	0.53	0.31	4.12
HDL Cholesterol (mmol/l)	1.49	0.34	0.67	2.59
LDL Cholesterol (mmol/l)	3.23	1.13	0.03	10.18
HDL Phosphatidyl choline (mmol/l)	1.39	0.29	0.55	2.41
Net Cholesterol (mmol/l)	5.12	1.10	2.69	11.13
LDL Apolipoprotein B (g/l) (n = 214)	0.857	0.237	0.292	1.955
Blood sugar (mmol/l)	5.10	0.67	3.28	11.66
Uric acid (µmol/l)	238	48	107	416
Cigarettes/day (n = 166 smokers)	15.9	8.5	1	50

cigarettes a day. Of the women, 34.8% were smokers with an average consumption of 15.9 cigarettes a day. Medium values, standard deviations and variation range of additional measured values and of laboratory parameters are given in tables 1 and 2.

Distribution of Lp(a) concentrations

For both sexes Lp(a) values had a similar high skewed distribution (tab. 3). In 14% of men and 12% of women values were below 0.02 g/l; 23% of men and 19% of women had values of 0.02 g/l, and 13% of men and 10% of women had values of 0.03 g/l. Only approx. 25% of all men and women had values >0.10 g/l. In both sexes, the proportion of subjects with Lp(a) concentrations of >0.25 g/l was 10%, 5% had Lp(a) concentrations >0.37 g/l. 6.5% of men and 6.1% of women had Lp(a) values >0.30 g/l.

Correlation of Lp(a) values to age

Whereas in men a correlation to age could not be statistically proven, there was a pronounced positive correlation of age to Lp(a) values in women ($r = 0.12$, $p < 0.001$), with a sudden increase in values for 40–50 year olds, i.e. approx. at the onset of the menopause. The medium value of Lp(a) in premenopausal women was 0.094 ± 0.129 g/l, in postmenopausal women it was 0.131 ± 0.171 g/l ($p < 0.001$). The proportion of subjects with raised Lp(a) values (>0.30 g/l) increased with the onset of the menopause from 4.1% to 11.3% ($p < 0.01$).

Tab. 3. Distribution of Lp(a) (g/l).
Prospective epidemiological study of company employees in Westfalia.

	Men (n = 987)	Women (n = 477)
Mean	0.100	0.104
Standard deviation	0.142	0.143
Median	0.039	0.050
Minimum	<0.01	<0.01
Maximum	0.93	1.00
70th percentile	0.09	0.09
75th percentile	0.11	0.12
80th percentile	0.16	0.16
85th percentile	0.21	0.20
90th percentile	0.25	0.24
95th percentile	0.37	0.37

Correlation of Lp(a) values to atherogenic risk factors (tab. 4)

In both sexes there was a positive correlation of Lp(a) concentrations to cholesterol, which was, however, more pronounced in women than in men (men: $r = 0.05$, $p < 0.05$; women: $r = 0.13$, $p < 0.01$); and also to LDL cholesterol (men: $r = 0.07$, $p < 0.01$; women: $r = 0.15$, $p < 0.001$), whereas only women showed a correlation of Lp(a) values and net cholesterol (= total cholesterol − Lp(a) cholesterol) ($r = 0.07$, $p < 0.05$). No significant correlation could be shown in either sex for Lp(a) to LDL apolipoprotein B.

Tab. 4. Coefficients of correlations between Lp(a) and risk factors.
Prospective epidemiological study of company employees in Westfalia.
987 men, 477 women.
* = $p < 0.05$
** = $p < 0.01$
*** = $p < 0.001$

	Men	Women
Age	−0.04	0.12***
Broca Index	−0.05*	0.10***
Systolic blood pressure	0.01	0.07*
Diastolic blood pressure	−0.02	0.01
Glucose	−0.04	0.04
Uric acid	0.00	−0.00
Cholesterol	0.05*	0.13***
Triglycerides	−0.04	0.02
HDL Cholesterol	0.06**	−0.05
HDL Phosphatidyl choline	0.02	−0.06
LDL Cholesterol	0.07**	0.15***
LDL Apolipoprotein B	−0.01 (n = 300)	0.09 (n = 214)
Cigarette smoking	−0.00 (n = 303)	0.02 (n = 166)
Net Cholesterol	−0.01	0.07*

There was an unexpected positive correlation in men of Lp(a) to HDL cholesterol ($r = 0.06$, $p < 0.01$) and a negative correlation to relative body weight (*Broca*) ($r = -0.05$, $p < 0.05$). Furthermore, in women, a positive correlation was observed of Lp(a) values to the *Broca* index ($r = 0.10$, $p < 0.01$), as well as Lp(a) values to systolic blood pressure ($r = 0.07$, $p < 0.05$). When the female subjects were divided into pre- and post-menopausal groups, the correlation of Lp(a) values to the systolic blood pressure disappeared, whereas the other correlations remained unchanged. No significant correlation of Lp(a) values to systolic blood pressure was observed in men. Neither sex showed statistically significant correlations of Lp(a) values to diastolic blood pressure, glucose, uric acid, triglycerides, HDL phosphatidyl choline or cigarette consumption.

Taking the Lp(a) concentration as an independent factor, the prevalence of the tested risk factors was compared in subjects with Lp(a) values >0.30 g/l (always mentioned first) and in those with Lp(a) values < = 0.30 g/l; the following results were obtained: The proportion of men with hypoalphalipoproteinaemia was significantly raised ($p < 0.01$) (28.1% as opposed to 14.3%; 15.6% as opposed to 5.3% when combined with hypertriglyceridaemia). In women the proportion of subjects with hypercholesterolaemia was 27.6% in the group with Lp(a) values >0.30 g/l, whereas only 7.6% of the remaining subjects showed hypercholesterolaemia. The corresponding values for hyperbetalipoproteinaemia were 24.1% compared to 5.5%. In both cases the proportion of affected subjects is significantly increased ($p < 0.001$). The proportion of female subjects showing Lp(a) values >0.30 g/l after the onset of the menopause was also significantly increased (51.7% compared to 26.3%; $p < 0.01$). Further remarkable but not significant differences were observed in men:

Hypercholesterolaemia 20.3% compared to 12.3%,

Hypertriglyceridaemia 25.0% compared to 16.8%,

Hyperbetalipoproteinaemia 15.6% compared to 8.9%.

Lp(a) values in hyperlipidaemic employees

The proportion of female subjects with raised Lp(a) values (>0.30 g/l) increased clearly with increasing cholesterol values (<5.70 mmol/l: 3.0%; 5.70–6.72 mmol/l: 10.8%; ≥6.73 mmol/l: 19.0%, $p < 0.001$), as well as with increasing LDL cholesterol values (LDL cholesterol <4.92 mmol/l: 5.0%; LDL cholesterol ≥4.92 mmol/l: 22.6%; $p < 0.001$). In men, the relative frequency of higher Lp(a) values was, however, not dependent on total cholesterol or LDL cholesterol levels (cholesterol <5.70 mmol/l: 5.5%; 5.70–6.72 mmol/l: 6.9%; ≥6.73 mmol/l: 10.3% (not significant); LDL cholesterol <4.92 mmol/l: 6.3%; ≥4.92 mmol/l: 11.2% (not significant)).

9.4% of the hypertriglyceridaemic men (triglycerides ≥2.28 mmol/l) had raised Lp(a) values (>0.30 g/l), and this proportion was marginally but not significantly higher than that in the remaining test group (5.9%).

In hypertriglyceridaemics with HDL cholesterol values <0.907 mmol/l, the prevalence of high Lp(a) values (>0.3 g/l) was higher than in the remaining test group (16.9% compared with 5.8%) ($p < 0.01$).

A general increase of Lp(a) values was, however, not observed in these individuals (median 0.02 g/l). Corresponding calculations for women were not feasible due to the low prevalence of hypertriglyceridaemia.

Discussion

An essential characteristic of Lp(a) lipoprotein is its markedly skewed distribution in the population. This has been shown by several authors (1, 5, 8, 16–18) and confirmed by us. The majority of the population obviously has relatively low Lp(a) concentrations, and higher Lp(a) values are found in only a few individuals. Individuals with Lp(a) values >0.30 g/l show corresponding "sinking pre-beta bands" in electrophoresis (19). It has been shown that the sinking pre-beta bands are passed on by autosomal dominant inheritance (19–21). In our tests, the median value for Lp(a) was about 0.04 g/l for men and 0.05 g/l for women; the 90th percentile was at 0.25 g/l (men) and 0.24 g/l (women); and the 95th percentile at 0.37 g/l (men), 0.35 g/l (women). These values are lower than those found by *Albers* et al. (1): median: 0.08 g/l, 90th percentile: 0.39 g/l, 95th percentile: 0.51 g/l; and by *Kostner* et al. (8): 80th percentile: 0.26 g/l, 90% percentile: 0.50 g/l. In the work of *Walton* et al. (16), however, the 95th percentile for a normal population was 0.20 g/l. The reason for this discrepancy in the frequency distribution of high Lp(a) values can on the one hand be due to the application of different standards in the Lp(a) analysis, on the other hand it could be due to real differences in the tested population.

Various research projects agree in their finding that patients with coronary heart disease have obviously higher Lp(a) values than healthy controls (6–8). *Kostner* et al. established a cut-off point at 0.3 g/l, above which an increased risk of coronary heart disease can be assumed (8). It has also been shown repeatedly, that Lp(a) has no bearing on known coronary risk factors, such as age, cholesterol, triglycerides (1, 8, 9) or cigarette consumption (10). However, the correlation of Lp(a) value and risk factors has so far only been tested on a relatively small scale in predominantly clinical orientated research, and to our knowledge, there are as yet no prospective epidemiological studies with larger numbers of subjects. Contrary to data published so far, we found a pronounced positive correlation of age to Lp(a) values in women. The division of the subjects into age groups showed, however, that the correlation results from a sharp increase in Lp(a) in 40–50 year old women, and is hence possibly related to the onset of the menopause. Since in >40–50 year old women LDL cholesterol values are also enhanced (22) and since in our results Lp(a) values are positively correlated with total cholesterol levels as well as with LDL cholesterol values one might speculate that the increase in Lp(a) values in post-menopausal women may be related to a common catabolic pathway of LDL and Lp(a). Based on the observation that the hepatic B, E receptor can be stimulated by pharmacological doses of oestrogen (23), changes in the plasma levels of LDL in postmenopausal women may be caused by reciprocal changes in the activity of the hepatic B, E receptor. At present, however, there are contradictory results with regard to the role of B, E receptors in the metabolism of Lp(a). According to findings of *Floren* et al. (24), Lp(a) was taken up mainly by the LDL receptor pathway, while according to the results of *Martmann-Moe & Berg* (25), Lp(a) was taken up independently of the LDL receptor pathway. Another indication for a different catabolic pathway of LDL and Lp(a) is the observation that in hypercholesterolaemic patients the application of cholestyramine only resulted in a reduction of the plasma LDL level without any change of the Lp(a) level (26).

Research by *Walton* et al. (16) or *Kostner* et al. (8) shows that individuals with hyperlipidaemia frequently have higher Lp(a) values than normolipidaemics. These observations were confirmed in our research: in subjects with hypertriglyceridaemia and hypoalphalipoproteinaemia there was a relatively higher proportion of subjects with Lp(a) values >0.30 g/l compared to normolipidaemics.

References

1. Albers, J. J., Cabana, V. G., Warnick, G. R. & Hazzard, W. R. (1975) Metabolism *24*, 1047–1054.
2. Simons, K., Ehnholm, C., Renkonen, O. & Bloth. B. (1970) Acta Pathol. Microbiol. Scand. *78*, 459–466.
3. Ehnholm, C., Garoff, H., Renkonen, O. & Simons, K. (1972) Biochemistry *11*, 3229–3232.
4. Krempler, F., Kostner, G., Bolzano, K. & Sandhofer, F. (1978) Atherosclerosis *30*, 57–65.
5. Albers, J. J., Adolphson, J. L. & Hazzard, W. R. (1977) J. Lipid Res. *18*, 331–338.
6. Dahlen, G., Berg, K. & Frick, M. H. (1976) Clin. Genet. *9*, 558–565.

7. Berg, K., Dahlen, G. & Borresen, A. L. (1979) Clin. Genet. *16*, 347–352.
8. Kostner, G. M., Avogaro, P., Cazzalato, G., Marth, E., Bittolo-Bon, G. & Quinci, G. B. (1981) Atherosclerosis *38*, 51–61.
9. Albers, J. J. & Hazzard, W. R. (1974) Lipids *9*, 15–26.
10. Dahlen, G., Berg, K., Ramberg, U.-B. & Tamm, A. (1974) Acta Med. Scand. *196*, 327–331.
11. Assmann, G., Oberwittler, W., Schulte, H., Schriewer, H., Funke, H., Epping, P. H. & Hauss, W. H. (1980) Internist *21*, 446–459.
12. Laurell, C. B. (1972) Scand. J. Clin. Lab. Invest. *29*, Suppl. 124, 21–37.
13. Assmann, G., Schriewer, H., Schmitz, G. & Hägele, E.-O. (1983) Clin. Chem. *29*, 2026–2030.
14. Schriewer, H., Jung, G., Emke, F. & Assmann, G. (1983) J. Clin. Chem. Clin. Biochem. *21*, 611–614.
15. Schriewer, H., Konert, U. & Assmann, G. (1984) J. Clin. Chem. Clin. Biochem. *22*, 35–40.
16. Walton, K. W., Hitchens, J., Magnani, H. N. & Khan, M. (1974) Atherosclerosis *20*, 323–346.
17. Marth, E., Cazzalato, G., Bittolo-Bon, G., Avogaro, P. & Kostner, G. M. (1982) Ann. Nutr. Metab. *26*, 56–62.
18. Molinari, E., Pichler, P., Krempler, F. & Kostner, G. M. (1983) Clin. Chim. Acta *128*, 373–378.
19. Pagnan, A., Kostner, G. M., Braggion, M., Ziron, L., Bittolo-Bon, G. & Avogaro, P. (1983) J. Clin. Chem. Clin. Biochem. *21*, 267–272.
20. Pagnan, A., Donadon, W. & Tonolli, E. (1974) Min. Med. *65*, 3123–3126.
21. Postle, A. E., Darmady, J. M. & Siggers, D. C. (1978) Clin. Genet. *13*, 233–236.
22. Assmann, G. In: Lipidstoffwechsel und Atherosklerose. Schattauer Verlag, Stuttgart, 1983.
23. Windler, E. E. T., Kovanen, P. T., Chao, Y.-S., Brown, M. S., Havel, R. J. & Goldstein, J. L. (1980) J. Biol. Chem. *255*, 10464–10471.
24. Floren, C. H., Albers, J. J. & Bierman, E. L. (1981) Biochem. Biophys. Res. Commun. *102*, 636–639.
25. Martmann-Moe, K. & Berg, K. (1981) Clin. Genet. *20*, 352–362.
26. Vessby, B., Kostner, G., Lithell, H. & Thomis, J. (1982) Atherosclerosis *44*, 61–71.

Professor Dr. H. Schriewer
Institut für Klinische Chemie und
Laboratoriumsmedizin (Zentrallaboratorium)
Medizinische Einrichtungen der
Westfälischen Wilhelms-Universität
Albert-Schweitzer-Straße 33
D-4400 Münster