

25	<a href="#">[Treatment of hypertension in patients with left ventricular hypertrophy]</a>	Tidsskr Nor Laegeforen 2004 Mar;124(6):788-91
26	<a href="#">Effects of losartan or atenolol in hypertensive patients without clinically evident vascular disease: a substudy of the LIFE randomized trial.</a>	Ann Intern Med 2003 Aug;139(3):169-77
27	<a href="#">Reducing cardiovascular morbidity and mortality in the elderly.</a>	Blood Press Suppl 2000;1 0:40-3
28	<a href="#">Outcomes in hypertensive patients at high cardiovascular risk treated with regimens based on valsartan or amlodipine: the VALUE randomised trial.</a>	Lancet 2004 Jun;363 (9426):2022-31
29	<a href="#">A calcium antagonist vs a non-calcium antagonist hypertension treatment strategy for patients with coronary artery disease. The International Verapamil-Trandolapril Study (INVEST): a randomized controlled trial.</a>	JAMA 2003 Dec;290 (21):2805-16
30	<a href="#">Prevention of heart failure by antihypertensive drug treatment in older persons with isolated systolic hypertension. SHEP Cooperative Research Group.</a>	JAMA 1997 Jul;278 (3):212-6
31	<a href="#">A comparison of outcomes with angiotensin-converting--enzyme inhibitors and diuretics for hypertension in the elderly.</a>	N Engl J Med 2003 Feb;348(7):583-92
32	<a href="#">Risks of untreated and treated isolated systolic hypertension in the elderly: meta-analysis of outcome trials.</a>	Lancet 2000 Mar;355 (9207):865-72
33	<a href="#">Stroke prevention with the angiotensin II type 1-receptor blocker candesartan in elderly patients with isolated systolic hypertension: the Study on Cognition and Prognosis in the Elderly (SCOPE).</a>	J Am Coll Cardiol 2004 Sep;44(6):1175-80
34	<a href="#">Reduced cardiovascular morbidity and mortality in hypertensive diabetic patients on first-line therapy with an ACE inhibitor compared with a diuretic/beta-blocker-based treatment regimen: a subanalysis of the Captopril Prevention Project.</a>	Diabetes Care 2001 Dec;24(12):2091-6
35	<a href="#">The stroke preventive effect in elderly hypertensives cannot fully be explained by the reduction in office blood pressure--insights from the Swedish Trial in Old Patients with Hypertension (STOP-Hypertension).</a>	Blood Press 1992 Oct;1 (3):168-72
36	<a href="#">The Losartan Intervention For Endpoint reduction (LIFE) in Hypertension study: rationale, design, and methods. The LIFE Study Group.</a>	Am J Hypertens 1997 Jul;10(7 Pt 1):705-13
37	<a href="#">Treatment of isolated systolic hypertension in the elderly: the Syst-Eur trial. Systolic Hypertension in Europe (Syst-Eur) Trial Investigators.</a>	Clin Exp Hypertens 1999 Jul-Aug;21(5-6):491-7
38	<a href="#">Medical Research Council trial of treatment of hypertension in older adults: principal results. MRC Working Party.</a>	BMJ 1992 Feb;304 (6824):405-12
39	<a href="#">Treatment of isolated systolic hypertension in the elderly: further evidence from the systolic hypertension in Europe (Syst-Eur) trial.</a>	Am J Cardiol 1998 Nov;82(9B):20R-22R
40	<a href="#">[The effect of losartan versus atenolol on cardiovascular morbidity and mortality in patients with diabetes mellitus in the LIFE-study]</a>	Ugeskr Laeger 2003 Jan;165(5):459-62
41	<a href="#">Predicting cardiovascular risk using conventional vs ambulatory blood pressure in older patients with systolic hypertension. Systolic Hypertension in Europe Trial Investigators.</a>	JAMA 1999 Aug;282 (6):539-46
42	<a href="#">Syst-Eur. A multicentre trial on the treatment of isolated systolic hypertension in the elderly: objectives, protocol, and organization.</a>	Ageing (Milano) 1991 Sep;3(3):287-302
43	<a href="#">STOP-Hypertension--preliminary communication from the pilot study of the Swedish Trial in Old Patients with Hypertension.</a>	J Hypertens Suppl 1987 Dec;5(5):S607-10
44	<a href="#">Calcium channel blockade and cardiovascular prognosis in the European trial on isolated systolic hypertension.</a>	Hypertension 1998 Sep;32(3):410-6
45	<a href="#">Comparison of antihypertensive treatments in preventing cardiovascular events in elderly diabetic patients: results from the Swedish Trial in Old Patients with Hypertension-2. STOP Hypertension-2 Study Group.</a>	J Hypertens 2000 Nov;18 (11):1671-5
46	<a href="#">[Effect of intensive antihypertensive treatment and of aspirin in a low dose in the hypertensive. The HOT (Hypertension Optimal Treatment) study]</a>	Arch Mal Coeur Vaiss 1999 Aug;92(8):1073-8
47	<a href="#">Treatment of mild hypertension: a five year controlled drug trial. The Oslo study.</a>	Am J Med 1980 Nov;69 (5):725-32
48	<a href="#">Major outcomes in high-risk hypertensive patients randomized to angiotensin-converting enzyme inhibitor or calcium channel blocker vs diuretic: The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT).</a>	JAMA 2002 Dec;288 (23):2981-97
49	<a href="#">Hypertension in the Very Elderly Trial (HYVET): protocol for the main trial.</a>	Drugs Aging 2001;18 (3):151-64
50	<a href="#">Treatment of isolated systolic hypertension: the SHELL study results.</a>	Blood Press 2003;12 (3):160-7

図 1 4 h 高血圧(04) 26～50位

高脂血症(05)

	Title	Journal
1	<a href="#">Primary prevention of acute coronary events with lovastatin in men and women with average cholesterol levels: results of AFCAPS/TexCAPS. Air Force/Texas Coronary Atherosclerosis Prevention Study.</a>	JAMA 1998 May;279 (20):1615-22
2	<a href="#">Large scale cohort study of the relationship between serum cholesterol concentration and coronary events with low-dose simvastatin therapy in Japanese patients with hypercholesterolemia and coronary heart disease: secondary prevention cohort study of the Japan Lipid Intervention Trial (J-LIT).</a>	Circ J 2002 Dec;66 (12):1096-100
3	<a href="#">Pravastatin in elderly individuals at risk of vascular disease (PROSPER): a randomised controlled trial.</a>	Lancet 2002 Nov;360 (9346):1623-30
4	<a href="#">Effects of pravastatin on coronary events in 2073 patients with low levels of both low-density lipoprotein cholesterol and high-density lipoprotein cholesterol: results from the LIPID study.</a>	Eur Heart J 2004 May;25 (9):771-7
5	<a href="#">Randomised trial of cholesterol lowering in 4444 patients with coronary heart disease: the Scandinavian Simvastatin Survival Study (4S).</a>	Lancet 1994 Nov;344 (8934):1363-9
6	<a href="#">Secondary prevention by raising HDL cholesterol and reducing triglycerides in patients with coronary artery disease: the Bezafibrate Infarction Prevention (BIP) study.</a>	Circulation 2000 Jul;102 (1):21-7
7	<a href="#">Air Force/Texas Coronary Atherosclerosis Prevention Study (AFCAPS/TexCAPS): efficacy and tolerability of long-term treatment with lovastatin in women.</a>	J Womens Health Gen Based Med 2001 Dec;10 (10):971-81
8	<a href="#">Achieving lipoprotein goals in patients at high risk with severe hypercholesterolemia: efficacy and safety of ezetimibe co-administered with atorvastatin.</a>	Am Heart J 2004 Sep;148 (3):447-55
9	<a href="#">Treatment with atorvastatin to the National Cholesterol Educational Program goal versus 'usual' care in secondary coronary heart disease prevention. The GREek Atorvastatin and Coronary-heart-disease Evaluation (GREACE) study.</a>	Curr Med Res Opin 2002;18(4):220-8
10	<a href="#">Influence of low high-density lipoprotein cholesterol and elevated triglyceride on coronary heart disease events and response to simvastatin therapy in 4S.</a>	Circulation 2001 Dec;104 (25):3046-51
11	<a href="#">Relation of gemfibrozil treatment and lipid levels with major coronary events: VA-HIT: a randomized controlled trial.</a>	JAMA 2001 Mar;285 (12):1585-91
12	<a href="#">Air Force/Texas Coronary Atherosclerosis Prevention Study (AFCAPS/TEXCAPS): additional perspectives on tolerability of long-term treatment with lovastatin.</a>	Am J Cardiol 2001 May;87(9):1074-9
13	<a href="#">Major outcomes in moderately hypercholesterolemic, hypertensive patients randomized to pravastatin vs usual care: The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT-LLT).</a>	JAMA 2002 Dec;288 (23):2998-3007
14	<a href="#">[Results of clinical epidemiology and intervention trial of hyperlipidemia in Japan]</a>	Nippon Rinsho 2002 May;60(5):889-98
15	<a href="#">Relationship between lipid levels and clinical outcomes in the Long-term Intervention with Pravastatin in Ischemic Disease (LIPID) Trial: to what extent is the reduction in coronary events with pravastatin explained by on-study lipid levels?</a>	Circulation 2002 Mar;105 (10):1162-9
16	<a href="#">Cholesterol levels after 3 days of high-dose simvastatin in patients at moderate to high risk for coronary events.</a>	Int J Cardiol 2005 May;101(1):111-4
17	<a href="#">Effectiveness of statin therapy in adults with coronary heart disease.</a>	Arch Intern Med 2004 Jul;164(13):1427-36
18	<a href="#">Effects of simvastatin on the lipid profile and attainment of low-density lipoprotein cholesterol goals when added to thiazolidinedione therapy in patients with type 2 diabetes mellitus: A multicenter, randomized, double-blind, placebo-controlled trial.</a>	Clin Ther 2004 Mar;26 (3):379-89
19	<a href="#">Effect of atorvastatin on high density lipoprotein cholesterol and its relationship with coronary events: a subgroup analysis of the GREek Atorvastatin and Coronary-heart-disease Evaluation (GREACE) Study.</a>	Curr Med Res Opin 2004 May;20(5):627-37
20	<a href="#">Effect of pravastatin on cardiovascular events in women after myocardial infarction: the cholesterol and recurrent events (CARE) trial.</a>	Lancet 2003 Apr;361 (9264):1149-58
21	<a href="#">Prevention of coronary and stroke events with atorvastatin in hypertensive patients who have average or lower-than-average cholesterol concentrations, in the Anglo-Scandinavian Cardiac Outcomes Trial-Lipid Lowering Arm (ASCOT-LLA): a multicentre randomised controlled trial.</a>	Drugs 2004;64 Suppl 2 0:43-60
22	<a href="#">Effect of pravastatin on cardiovascular events in women after myocardial infarction: the cholesterol and recurrent events (CARE) trial.</a>	J Am Coll Cardiol 1998 Jul;32(1):140-6
23	<a href="#">The Lipid Research Clinics Coronary Primary Prevention Trial results. I. Reduction in incidence of coronary heart disease.</a>	JAMA 1984 Jan;251 (3):351-64
24	<a href="#">Twelve-week, multicenter, randomized, open-label comparison of the effects of rosuvastatin 10 mg/d and atorvastatin 10 mg/d in high-risk adults: a DISCOVERY study.</a>	Clin Ther 2004 Nov;26 (11):1821-33
25	<a href="#">The effect of pravastatin on coronary events after myocardial infarction in patients with average cholesterol levels. Cholesterol and Recurrent Events Trial investigators.</a>	N Engl J Med 1996 Oct;335(14):1001-9

図 1 4 i 高脂血症(05) 1 ~ 2 5 位

25	<a href="#">The effect of pravastatin on coronary events after myocardial infarction in patients with average cholesterol levels. Cholesterol and Recurrent Events Trial investigators.</a>	N Engl J Med 1996 Oct;335(14):1001-9
26	<a href="#">The effect of pravastatin on coronary events after myocardial infarction in patients with average cholesterol levels. Cholesterol and Recurrent Events Trial Study.</a>	N Engl J Med 1996 Aug;341(8):413-8
27	<a href="#">HDL cholesterol predicts coronary heart disease mortality in older persons.</a>	JAMA 1995 Aug;274(7):539-44
28	<a href="#">Lipoprotein changes and reduction in the incidence of major coronary heart disease events in the Scandinavian Simvastatin Survival Study (4S).</a>	Circulation 1998 Apr;97(15):1453-60
29	<a href="#">MRC/BHF Heart Protection Study of cholesterol lowering with simvastatin in 20,536 high-risk individuals: a randomised placebo-controlled trial.</a>	Lancet 2002 Jul;360(9326):7-22
30	<a href="#">Effect of pravastatin on cardiovascular events in older patients with myocardial infarction and cholesterol levels in the average range. Results of the Cholesterol and Recurrent Events (CARE) trial.</a>	Ann Intern Med 1998 Nov;129(9):681-9
31	<a href="#">The collaborative atorvastatin diabetes study: preliminary results.</a>	Int J Clin Pract 2005 Jan;59(1):121-3
32	<a href="#">A comparison of the efficacy and tolerability of titrate-to-goal regimens of simvastatin and fluvastatin: a randomized, double-blind study in adult patients at moderate to high risk for cardiovascular disease.</a>	Clin Ther 2001 Mar;23(3):467-78
33	<a href="#">Cholesterol-lowering therapy in women and elderly patients with myocardial infarction or angina pectoris: findings from the Scandinavian Simvastatin Survival Study (4S).</a>	Circulation 1997 Dec;96(12):4211-8
34	<a href="#">Safety of low-density lipoprotein cholesterol reduction with atorvastatin versus simvastatin in a coronary heart disease population (the TARGET TANGIBLE trial).</a>	Am J Cardiol 1999 Jul;84(1):7-13
35	<a href="#">Design &amp; rationale of the Air Force/Texas Coronary Atherosclerosis Prevention Study (AFCAPS/TexCAPS).</a>	Am J Cardiol 1997 Aug;80(3):287-93
36	<a href="#">Effects of low doses of simvastatin and atorvastatin on high-density lipoprotein cholesterol levels in patients with hypercholesterolemia.</a>	Clin Ther 2001 Jun;23(6):851-7
37	<a href="#">Gemfibrozil for secondary prevention of cardiovascular events in mild to moderate chronic renal insufficiency.</a>	Kidney Int 2004 Sep;66(3):1123-30
38	<a href="#">Reducing the risk of coronary events: evidence from the Scandinavian Simvastatin Survival Study (4S).</a>	Am J Cardiol 1995 Sep;76(9):64C-68C
39	<a href="#">Effects of ezetimibe added to on-going statin therapy on the lipid profile of hypercholesterolemic patients with diabetes mellitus or metabolic syndrome.</a>	Curr Med Res Opin 2004 Sep;20(9):1437-45
40	<a href="#">Effect of pravastatin on coronary disease events in subgroups defined by coronary risk factors: the Prospective Pravastatin Pooling Project.</a>	Circulation 2000 Oct;102(16):1893-900
41	<a href="#">Cardiovascular events and their reduction with pravastatin in diabetic and glucose-intolerant myocardial infarction survivors with average cholesterol levels: subgroup analyses in the cholesterol and recurrent events (CARE) trial. The Care Investigators.</a>	Circulation 1998 Dec;98(23):2513-9
42	<a href="#">Coaching patients with coronary heart disease to achieve the target cholesterol: a method to bridge the gap between evidence-based medicine and the "real world"—randomized controlled trial.</a>	J Clin Epidemiol 2002 Mar;55(3):245-52
43	<a href="#">Design and baseline characteristics of the Incremental Decrease in End Points through Aggressive Lipid Lowering study.</a>	Am J Cardiol 2004 Sep;94(6):720-4
44	<a href="#">Effect of pravastatin on cardiovascular events and mortality in 1516 women with coronary heart disease: results from the Long-Term Intervention with Pravastatin in Ischemic Disease (LIPID) study.</a>	Am Heart J 2003 Apr;145(4):643-51
45	<a href="#">Efficacy and safety of pravastatin in the long-term treatment of elderly patients with hypercholesterolemia.</a>	Am J Med 1994 Jun;96(6):509-15
46	<a href="#">[Statin therapy for hypertensive patients]</a>	Tidsskr Nor Lægeforen 2004 Jan;124(2):166-6
47	<a href="#">The relationship between low-density lipoprotein cholesterol goal attainment and prevention of coronary heart disease-related events.</a>	J Cardiovasc Pharmacol Ther 2001 Apr;6(2):129-35
48	<a href="#">Effects of simvastatin versus gemfibrozil on lipids and glucose control in patients with non-insulin-dependent diabetes mellitus. NIDDM Study Group.</a>	Clin Ther 1995 Mar-Apr;17(2):186-203
49	<a href="#">Diabetes, plasma insulin, and cardiovascular disease: subgroup analysis from the Department of Veterans Affairs high-density lipoprotein intervention trial (VA-HIT).</a>	Arch Intern Med 2002 Dec 9-23;162(22):2597-604
50	<a href="#">Cholesterol lowering with simvastatin improves prognosis of diabetic patients with coronary heart disease. A subgroup analysis of the Scandinavian Simvastatin Survival Study (4S).</a>	Diabetes Care 1997 Apr;20(4):614-20

図 1 4 j 高脂血症(05) 26~50位

その他(06) (糖尿病, 脳卒中, 複合領域ほか)

	Title	Journal
1	<u>Multifactorial intervention and cardiovascular disease in patients with type 2 diabetes.</u>	N Engl J Med 2003 Jan;348(5):383-93
2	<u>Effects of losartan on renal and cardiovascular outcomes in patients with type 2 diabetes and nephropathy.</u>	N Engl J Med 2001 Sep;345(12):861-9
3	<u>The effect of nisoldipine as compared with enalapril on cardiovascular outcomes in patients with non-insulin-dependent diabetes and hypertension.</u>	N Engl J Med 1998 Mar;338(10):645-52
4	<u>Primary prevention of cardiovascular disease with atorvastatin in type 2 diabetes in the Collaborative Atorvastatin Diabetes Study (CARDS): multicentre randomised placebo-controlled trial.</u>	Lancet 2004 Aug 21-27;364(9436):685-96
5	<u>Renoprotective effect of the angiotensin-receptor antagonist irbesartan in patients with nephropathy due to type 2 diabetes.</u>	N Engl J Med 2001 Sep;345(12):861-60
6	<u>Effects of low dose ramipril on cardiovascular and renal outcomes in patients with type 2 diabetes and raised excretion of urinary albumin: randomised, double blind, placebo controlled trial (the DIABHYCAR study).</u>	BMJ 2004 Feb;328(7438):495
7	<u>A randomized trial of low-dose aspirin in the primary prevention of cardiovascular disease in women.</u>	N Engl J Med 2005 Mar;352(13):1293-304
8	<u>Atorvastatin in patients with type 2 diabetes mellitus undergoing hemodialysis.</u>	N Engl J Med 2005 Jul;353(3):238-48
9	<u>Tight blood pressure control and risk of macrovascular and microvascular complications in type 2 diabetes: UKPDS 38. UK Prospective Diabetes Study Group.</u>	BMJ 1998 Sep;317(7160):703-13
10	<u>[Effect of losartan on renal and cardiovascular complications of patients with type 2 diabetes and nephropathy]</u>	Ugeskr Laeger 2001 Oct;163(40):5514-9
11	<u>Aspirin and ticlopidine for prevention of recurrent stroke in black patients: a randomized trial.</u>	JAMA 2003 Jun;289(22):2947-57
12	<u>Cardiovascular morbidity and mortality in the Losartan Intervention For Endpoint reduction in hypertension study (LIFE): a randomised trial against atenolol.</u>	Lancet 2002 Mar;359(9311):995-1003
13	<u>Effects of ramipril on cardiovascular and microvascular outcomes in people with diabetes mellitus: results of the HOPE study and MICRO-HOPE substudy. Heart Outcomes Prevention Evaluation Study Investigators.</u>	Lancet 2000 Jan;355(9200):253-9
14	<u>Effects of an angiotensin-converting-enzyme inhibitor, ramipril, on cardiovascular events in high-risk patients. The Heart Outcomes Prevention Evaluation Study Investigators.</u>	N Engl J Med 2000 Jan;342(3):145-53
15	<u>Effects of an angiotensin-converting-enzyme inhibitor, ramipril, on cardiovascular events in high-risk patients. The Heart Outcomes Prevention Evaluation Study Investigators.</u>	N Engl J Med 2000 Jan;342(3):145-53
16	<u>Outcome results of the Fosinopril Versus Amlodipine Cardiovascular Events Randomized Trial (FACET) in patients with hypertension and NIDDM.</u>	Diabetes Care 1998 Apr;21(4):597-603
17	<u>Trial of secondary prevention with atenolol after transient ischemic attack or nondisabling ischemic stroke. The Dutch TIA Trial Study Group.</u>	Stroke 1993 Apr;24(4):543-8
18	<u>The Study on Cognition and Prognosis in the Elderly (SCOPE): principal results of a randomized double-blind intervention trial.</u>	J Hypertens 2003 May;21(5):875-86
19	<u>Efficacy and safety of low-dose aspirin in polycythemia vera.</u>	N Engl J Med 2004 Jan;350(2):114-24
20	<u>A comparison of warfarin and aspirin for the prevention of recurrent ischemic stroke.</u>	N Engl J Med 2001 Nov;345(20):1444-51
21	<u>PROGRESS: Perindopril pROtection aGainst REcurrent Stroke Study: status in March 1997. PROGRESS Management Committee.</u>	J Hum Hypertens 1998 Sep;12(9):627-9
22	<u>New evidence on the prevention of cardiovascular events in hypertensive patients with type 2 diabetes.</u>	J Cardiovasc Pharmacol 1998;32 Suppl 20:S18-23
23	<u>Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). UK Prospective Diabetes Study (UKPDS) Group.</u>	Lancet 1998 Sep;352(9131):837-53
24	<u>Effects of an angiotensin-converting-enzyme inhibitor, ramipril, on cardiovascular events in high-risk patients. The Heart Outcomes Prevention Evaluation Study Investigators.</u>	N Engl J Med 2000 Jan;342(3):145-53
25	<u>The effect of irbesartan on the development of diabetic nephropathy in patients with type 2 diabetes.</u>	N Engl J Med 2001 Sep;345(12):870-8

図 1 4 k その他(06) (糖尿病, 脳卒中, 複合領域ほか) 1 ~ 2 5 位

25	<a href="#">The effect of irbesartan on the development of diabetic nephropathy in patients with type 2 diabetes.</a>	N Engl J Med 2001 Sep;345(12):870-8
26	<a href="#">Cardiovascular outcomes in the Irbesartan Diabetic Nephropathy Trial of patients with type 2 diabetes and overt nephropathy.</a>	Ann Intern Med 2003 Apr;138(7):542-9
27	<a href="#">Vitamin E supplementation and cardiovascular events in high-risk patients. The Heart Outcomes Prevention Evaluation Study Investigators.</a>	N Engl J Med 2000 Jan;342(3):154-60
28	<a href="#">Effect of ramipril vs amlodipine on renal outcomes in hypertensive nephrosclerosis: a randomized controlled trial.</a>	Lancet 1998 Jun;351 181:1755-62
29	<a href="#">Effect of ramipril vs amlodipine on renal outcomes in hypertensive nephrosclerosis: a randomized controlled trial.</a>	JAMA 2001 Jun;285 (21):2719-28
30	<a href="#">Aspirin and clopidogrel compared with clopidogrel alone after recent ischaemic stroke or transient ischaemic attack in high-risk patients (MATCH): randomised, double-blind, placebo-controlled trial.</a>	Lancet 2004 Jul 24- 30;364(9431):331-7
31	<a href="#">Effects of cholesterol-lowering with simvastatin on stroke and other major vascular events in 20536 people with cerebrovascular disease or other high-risk conditions.</a>	Lancet 2004 Mar;363 (9411):757-67
32	<a href="#">Randomised trial of a perindopril-based blood-pressure-lowering regimen among 6105 individuals with previous stroke or transient ischaemic attack.</a>	Lancet 2001 Sep;358 (9287):1033-41
33	<a href="#">Risk factors for stroke and efficacy of antithrombotic therapy in atrial fibrillation. Analysis of pooled data from five randomized controlled trials.</a>	Arch Intern Med 1994 Jul;154(13):1449-57
34	<a href="#">Primary prevention of cardiovascular events with low-dose aspirin and vitamin E in type 2 diabetic patients: results of the Primary Prevention Project (PPP) trial.</a>	Diabetes Care 2003 Dec;26(12):3264-72
35	<a href="#">Randomised trial of effects of calcium antagonists compared with diuretics and beta-blockers on cardiovascular morbidity and mortality in hypertension: the Nordic Diltiazem (NORDIL) study.</a>	Lancet 2000 Jul;356 (9227):359-65
36	<a href="#">Antiplatelet therapy for preventing stroke in patients with nonrheumatic atrial fibrillation and a history of stroke or transient ischemic attacks.</a>	Cochrane Database Syst Rev 2000;(2):CD000186
37	<a href="#">Effects of losartan or atenolol in hypertensive patients without clinically evident vascular disease: a substudy of the LIFE randomized trial.</a>	Ann Intern Med 2003 Aug;139(3):169-77
38	<a href="#">A clinical trial in type 2 diabetic nephropathy.</a>	Am J Kidney Dis 2001 Oct;38(4 Suppl 1):S191-4
39	<a href="#">Comparison of warfarin and aspirin for symptomatic intracranial arterial stenosis.</a>	N Engl J Med 2005 Mar;352(13):1305-16
40	<a href="#">Dipyridamole for preventing stroke and other vascular events in patients with vascular disease.</a>	Cochrane Database Syst Rev 2003;(1):CD001820
41	<a href="#">Relation between renal dysfunction and cardiovascular outcomes after myocardial infarction.</a>	N Engl J Med 2004 Sep;351(13):1285-95
42	<a href="#">Effects of losartan on renal and cardiovascular outcomes in patients with nephropathy.</a>	Am Heart J 2003 Dec;146(6):E20
43	<a href="#">Randomised double-blind comparison of placebo and active treatment for older patients with isolated systolic hypertension. The Systolic Hypertension in Europe (Syst-Eur) Trial Investigators.</a>	Lancet 1997 Sep;350 (9080):757-64
44	<a href="#">Effects of losartan on renal and cardiovascular outcomes in patients with nephropathy.</a>	Lancet 2003 Apr;361 (9364):1193-9
45	<a href="#">Effects of losartan on renal and cardiovascular outcomes in patients with nephropathy.</a>	Lancet 1998 Nov;354 9132:1751-6
46	<a href="#">Prevention of coronary and stroke events with atorvastatin in hypertensive patients who have average or lower-than-average cholesterol concentrations, in the Anglo-Scandinavian Cardiac Outcomes Trial--Lipid Lowering Arm (ASCOT-LLA): a multicentre randomised controlled trial.</a>	Drugs 2004;64 Suppl 2 0:43-60
47	<a href="#">PROGRESS (perindopril protection against recurrent stroke study): rationale and design. PROGRESS Management Committee [corrected]</a>	J Hypertens 1995 Dec;13 (12 Pt 2):1869-73
48	<a href="#">Morbidity and mortality in patients randomised to double-blind treatment with a long-acting calcium-channel blocker or diuretic in the International Nifedipine GIT5 study: Intervention as a Goal in Hypertension Treatment (INSIGHT).</a>	Lancet 2000 Jul;356 (9227):366-72
49	<a href="#">PROGRESS--perindopril protection against recurrent stroke study: status in July 1996. PROGRESS Management Committee.</a>	J Hypertens Suppl 1996 Dec;14(6):S47-51
50	<a href="#">A randomised, blinded, trial of clopidogrel versus aspirin in patients at risk of ischaemic events (CAPRIE). CAPRIE Steering Committee.</a>	Lancet 1996 Nov;348 (9038):1329-39

図 1 4 L その他(06) (糖尿病, 脳卒中, 複合領域ほか) 26 ~ 50位

メタアナリシス(07)

	Title	Journal
1	<u>Intravenous glycoprotein IIb/IIIa receptor antagonists reduce mortality after percutaneous coronary interventions.</u>	J Am Coll Cardiol 2003 Jan;41(1):26-32
2	<u>Early vs late administration of glycoprotein IIb/IIIa inhibitors in primary percutaneous coronary intervention of acute ST-segment elevation myocardial infarction: a meta-analysis.</u>	JAMA 2004 Jul;292(3):362-6
3	<u>Platelet glycoprotein IIb/IIIa inhibitors in acute coronary syndromes: a meta-analysis of all major randomised clinical trials.</u>	Lancet 2002 Jan;359(9302):189-98
4	<u>Health outcomes associated with calcium antagonists compared with other first-line antihypertensive therapies: a meta-analysis of randomised controlled trials.</u>	Lancet 2000 Dec;356(9246):1949-54
5	<u>Health outcomes associated with various antihypertensive therapies used as first-line agents: a network meta-analysis.</u>	JAMA 2003 May;289(19):2534-44
6	<u>Direct thrombin inhibitors in acute coronary syndromes: principal results of a meta-analysis based on individual patients' data.</u>	Lancet 2002 Jan;359(9303):294-302
7	<u>Improved clinical outcomes with abciximab therapy in acute myocardial infarction: a systematic overview of randomized clinical trials.</u>	Am Heart J 2004 Mar;147(3):457-62
8	<u>Effect of angiotensin converting enzyme inhibition on sudden cardiac death in patients following acute myocardial infarction. A meta-analysis of randomized clinical trials.</u>	J Am Coll Cardiol 1999 Mar;33(3):598-604
9	<u>Clinical outcomes of therapeutic agents that block the platelet glycoprotein IIb/IIIa integrin in ischemic heart disease.</u>	Circulation 1998 Dec 22-29;98(25):2829-35
10	<u>Meta-analysis of survival with platelet glycoprotein IIb/IIIa antagonists for percutaneous coronary interventions.</u>	Am J Cardiol 2003 Sep;92(6):651-5
11	<u>Use of statins in primary and secondary prevention of coronary heart disease and ischemic stroke. Meta-analysis of randomized trials.</u>	Int J Clin Pharmacol Ther 2003 Dec;41(12):567-77
12	<u>[The clinical use of the GPIIb/IIIa inhibitors eptifibatid and tirofiban in the treatment of acute coronary syndromes of the "non-ST elevation" type]</u>	Ital Heart J Suppl 2000 Feb;1(2):202-11
13	<u>Implantable defibrillators for the prevention of mortality in patients with nonischemic cardiomyopathy: a meta-analysis of randomized controlled trials.</u>	JAMA 2004 Dec;292(23):2874-9
14	<u>Platelet glycoprotein IIb/IIIa inhibitors reduce mortality in diabetic patients with non-ST-segment-elevation acute coronary syndromes.</u>	Circulation 2001 Dec;104(23):2767-71
15	<u>Effect of statins on risk of coronary disease: a meta-analysis of randomized controlled trials.</u>	JAMA 1999 Dec 22-29;282(24):2340-6
16	<u>Effect of prophylactic amiodarone on mortality after acute myocardial infarction and in congestive heart failure: meta-analysis of individual data from 6500 patients in randomised trials. Amiodarone Trials Meta-Analysis Investigators.</u>	Lancet 1997 Nov;350(9089):1417-24
17	<u>Efficacy and safety of abciximab on acute myocardial infarction treated with percutaneous coronary interventions: a meta-analysis of randomized controlled trials.</u>	Am Heart J 2004 Dec;148(6):937-43
18	<u>The failure of orally administered glycoprotein IIb/IIIa inhibitors to prevent recurrent cardiac events.</u>	Am J Med 2002 Jun;112(8):647-58
19	<u>Health outcomes associated with antihypertensive therapies used as first-line agents. A systematic review and meta-analysis.</u>	JAMA 1997 Mar;277(9):739-45
20	<u>Increased mortality with oral platelet glycoprotein IIb/IIIa antagonists: a meta-analysis of phase III multicenter randomized trials.</u>	Circulation 2001 Jan;103(2):201-6
21	<u>Effects of ACE inhibitors, calcium antagonists, and other blood-pressure-lowering drugs: results of prospectively designed overviews of randomised trials. Blood Pressure Lowering Treatment Trialists' Collaboration.</u>	Lancet 2000 Dec;356(9246):1955-64
22	<u>Warfarin plus aspirin after myocardial infarction or the acute coronary syndrome: meta-analysis with estimates of risk and benefit.</u>	Ann Intern Med 2005 Aug;143(4):241-50
23	<u>Routine vs selective invasive strategies in patients with acute coronary syndromes: a collaborative meta-analysis of randomized trials.</u>	JAMA 2005 Jun;293(23):2908-17
24	<u>Long-term ACE-inhibitor therapy in patients with heart failure or left-ventricular dysfunction: a systematic overview of data from individual patients. ACE-Inhibitor Myocardial Infarction Collaborative Group.</u>	Lancet 2000 May;355(9215):1575-81
25	<u>Overview of randomized trials of angiotensin-converting enzyme inhibitors on mortality and morbidity in patients with heart failure. Collaborative Group on ACE Inhibitor Trials.</u>	JAMA 1995 May;273(18):1450-6

図 1 4 m メタアナリシス(07) 1～25位

25	<u>Overview of randomized trials of angiotensin-converting enzyme inhibitors on mortality and morbidity in patients with heart failure. Collaborative Group on ACE Inhibitor Trials.</u>	JAMA 1995 May;273(18):1450-6
26	<u>Effect of beta-blockade on mortality in patients with heart failure: a meta-analysis of randomized clinical trials.</u>	J Am Coll Cardiol 1997 Jul;30(1):27-34
27	<u>Effects of different blood-pressure-lowering regimens on major cardiovascular events: results of prospectively-designed overviews of randomised trials.</u>	Lancet 2003 Nov;362(9396):1527-35
28	<u>Effect of HMGCoA reductase inhibitors on stroke. A meta-analysis of randomized, controlled trials.</u>	Ann Intern Med 1998 Jan;128(2):89-95
29	<u>Clinical outcomes in statin treatment trials: a meta-analysis.</u>	Arch Intern Med 1999 Aug 9-23;159(15):1793-802
30	<u>Current evidence supporting the role of diuretics in heart failure: a meta analysis of randomised controlled trials.</u>	Int J Cardiol 2002 Feb;82(2):149-58
31	<u>Effects of antibiotic therapy on outcomes of patients with coronary artery disease: a meta-analysis of randomized controlled trials.</u>	JAMA 2005 Jun;293(21):2641-7
32	<u>Effect of glycoprotein IIb/IIIa inhibitors on the individual components of composite endpoints used in clinical trials of unstable angina and non-Q-wave myocardial infarction.</u>	Cardiovasc Drugs Ther 2000 Jun;14(3):253-8
33	<u>Platelet glycoprotein IIb/IIIa blockers for percutaneous coronary revascularization, and unstable angina and non-ST-segment elevation myocardial infarction.</u>	Cochrane Database Syst Rev 2001;(4):CD002130
34	<u>Cardiac resynchronization and death from progressive heart failure: a meta-analysis of randomized controlled trials.</u>	JAMA 2003 Feb;289(6):730-40
35	<u>[Does statin therapy reduce the risk of stroke? A meta-analysis]</u>	Ann Med Interne (Paris) 2001 Apr;152(3):188-93
36	<u>Cardiovascular protection and blood pressure reduction: a meta-analysis.</u>	Lancet 2001 Oct;358(9290):1305-15
37	<u>Transfer for primary angioplasty versus immediate thrombolysis in acute myocardial infarction: a meta-analysis.</u>	Circulation 2003 Oct;108(15):1809-14
38	<u>Lack of benefit from intravenous platelet glycoprotein IIb/IIIa receptor inhibition as adjunctive treatment for percutaneous interventions of aortocoronary bypass grafts: a pooled analysis of five randomized clinical trials.</u>	Circulation 2002 Dec;106(24):3063-7
39	<u>Effects of acadesine on myocardial infarction, stroke, and death following surgery. A meta-analysis of the 5 international randomized trials. The Multicenter Study of Perioperative Ischemia (McSPD) Research Group.</u>	JAMA 1997 Jan 22-29;277(4):325-32
40	<u>Risks and benefits of glycoprotein IIb/IIIa antagonists in acute coronary syndrome.</u>	Ann Pharmacother 2001 Apr;35(4):472-9
41	<u>Effect of glycoprotein IIb/IIIa receptor blocker abciximab on outcome in patients with acute coronary syndromes without early coronary revascularisation: the GUSTO IV-ACS randomised trial.</u>	Lancet 2001 Jun;357(9272):1915-24
42	<u>Primary stenting versus primary balloon angioplasty for treating acute myocardial infarction.</u>	Cochrane Database Syst Rev 2005;(2):CD005313
43	<u>Comparison of primary coronary angioplasty and intravenous thrombolytic therapy for acute myocardial infarction: a quantitative review.</u>	JAMA 1997 Dec;278(23):2093-8
44	<u>Safety outcomes in meta-analyses of phase 2 vs phase 3 randomized trials: Intracranial hemorrhage in trials of bolus thrombolytic therapy.</u>	JAMA 2001 Jan 24-31;285(4):444-50
45	<u>Thrombolysis for acute ischaemic stroke.</u>	Cochrane Database Syst Rev 2003;(3):CD000213
46	<u>Angioplasty and stents in coronary artery disease: a systematic review and meta-analysis.</u>	Scand Cardiovasc J 2004 Aug;38(4):200-10
47	<u>Cholesterol lowering with statin drugs, risk of stroke, and total mortality. An overview of randomized trials.</u>	JAMA 1997 Jul 23-30;278(4):313-21
48	<u>Effect of smoking status and abciximab use on outcome after percutaneous coronary revascularization: Pooled analysis from EPIC, EPICLOG, and EPISTENT.</u>	Am Heart J 2001 Apr;141(4):599-602
49	<u>Clinical outcomes of bivalirudin for ischemic heart disease.</u>	Circulation 1999 Nov;100(20):2049-53
50	<u>Amiodarone prophylaxis reduces major cardiovascular morbidity and length of stay after cardiac surgery: a meta-analysis.</u>	Ann Intern Med 2005 Sep;143(5):327-36

図 1 4 n メタアナリシス(07) 26～50位

	Title	Journal
1	<a href="#">Characteristics of 9194 patients with left ventricular hypertrophy: the LIFE study. Losartan Intervention For Endpoint Reduction in Hypertension.</a>	Hypertension 1998 Dec;32(6):989-97
2	<a href="#">Trends in the incidence of outcomes defining acquired immunodeficiency syndrome (AIDS) in the Multicenter AIDS Cohort Study: 1985-1991.</a>	Am J Epidemiol 1993 Feb;137(4):423-38
3	<a href="#">Impaired glucose tolerance in obesity is associated with insensitivity to insulin in multiple aspects of metabolism as assessed by a low dose incremental insulin infusion technique.</a>	Diabet Med 1991 Oct;8(8):718-25
4	<a href="#">The independent effect of type 2 diabetes mellitus on ischemic heart disease, stroke, and death: a population-based study of 13,000 men and women with 20 years of follow-up.</a>	Arch Intern Med 2004 Jul;164(13):1422-6
5	<a href="#">The Losartan Intervention For Endpoint reduction (LIFE) in Hypertension study: rationale, design, and methods. The LIFE Study Group.</a>	Am J Hypertens 1997 Jul;10(7 Pt 1):705-13
6	<a href="#">Regression of electrocardiographic left ventricular hypertrophy by losartan versus atenolol: The Losartan Intervention for Endpoint reduction in Hypertension (LIFE) Study.</a>	Circulation 2003 Aug;108(6):684-90
7	<a href="#">Regression of electrocardiographic left ventricular hypertrophy during antihypertensive treatment and the prediction of major cardiovascular events.</a>	JAMA 2004 Nov;292(19):2343-9
8	<a href="#">Baseline characteristics in relation to electrocardiographic left ventricular hypertrophy in hypertensive patients: the Losartan intervention for endpoint reduction (LIFE) in hypertension study. The Life Study Investigators.</a>	Hypertension 2000 Nov;36(5):766-73
9	<a href="#">Population impact of losartan use on stroke in the European Union (EU): projections from the Losartan Intervention For Endpoint reduction in hypertension (LIFE) study.</a>	J Hum Hypertens 2004 Jun;18(6):367-73
10	<a href="#">Cardiovascular morbidity and mortality in the Losartan Intervention For Endpoint reduction in hypertension study (LIFE): a randomised trial against atenolol.</a>	Lancet 2002 Mar;359(9311):995-1003
11	<a href="#">Effects of losartan on cardiovascular morbidity and mortality in patients with isolated systolic hypertension and left ventricular hypertrophy: a Losartan Intervention for Endpoint Reduction (LIFE) substudy.</a>	JAMA 2002 Sep;288(12):1491-8
12	<a href="#">Relation of QT interval and QT dispersion to regression of echocardiographic and electrocardiographic left ventricular hypertrophy in hypertensive patients: the Losartan Intervention For Endpoint Reduction (LIFE) study.</a>	Am Heart J 2003 May;145(5):919-25
		Lancet 2002 Mar;359(9311):1004-10
14	<a href="#">Effects of losartan or atenolol in hypertensive patients without clinically evident vascular disease: a substudy of the LIFE randomized trial.</a>	Ann Intern Med 2003 Aug;139(3):169-77
15	<a href="#">Progressive hypertrophy regression with sustained pressure reduction in hypertension: the Losartan Intervention For Endpoint Reduction study.</a>	J Hypertens 2002 Jul;20(7):1445-50
16	<a href="#">Relation of echocardiographic left ventricular mass and hypertrophy to persistent electrocardiographic left ventricular hypertrophy in hypertensive patients: the LIFE Study.</a>	Am J Hypertens 2001 Aug;14(8 Pt 1):775-82
17	<a href="#">Regression of hypertensive left ventricular hypertrophy by losartan compared with atenolol: the Losartan Intervention for Endpoint Reduction in Hypertension (LIFE) trial.</a>	Circulation 2004 Sep;110(11):1456-62
18	<a href="#">The Effect of Losartan Versus Atenolol on Cardiovascular Morbidity and Mortality in Patients With Hypertension Taking Aspirin The Losartan Intervention for Endpoint Reduction in Hypertension (LIFE) Study.</a>	J Am Coll Cardiol 2005 Sep;46(5):770-5
19	<a href="#">Lowering of blood pressure and predictors of response in patients with left ventricular hypertrophy: the LIFE study. Losartan Intervention For Endpoint.</a>	Am J Hypertens 2000 Aug;13(8):899-906
20	<a href="#">QRS duration and QT interval predict mortality in hypertensive patients with left ventricular hypertrophy: the Losartan Intervention for Endpoint Reduction in Hypertension Study.</a>	Hypertension 2004 May;43(5):1029-34
21	<a href="#">Risk of new-onset diabetes in the Losartan Intervention For Endpoint reduction in hypertension study.</a>	J Hypertens 2002 Sep;20(9):1879-86
22	<a href="#">Use of losartan in diabetic patients in the primary care setting: review of the results in LIFE and RENAAL.</a>	Curr Med Res Opin 2004 Dec;20(12):1909-17
23	<a href="#">The stroke volume/pulse pressure ratio predicts coronary heart disease mortality in a population of elderly men.</a>	J Hypertens 2004 May;22(5):899-906
24	<a href="#">Cardiovascular morbidity and mortality in hypertensive patients with a history of atrial fibrillation: The Losartan Intervention For End Point Reduction in Hypertension (LIFE) study.</a>	J Am Coll Cardiol 2005 Mar;45(5):705-11
25	<a href="#">The effects of losartan compared to atenolol on stroke in patients with isolated systolic hypertension and left ventricular hypertrophy. The LIFE study.</a>	J Clin Hypertens (Greenwich) 2005 Mar;7(3):152-8

図 1 4 p 疫学(09) 1 ~ 2 5 位



25	<a href="#">The effects of losartan compared to atenolol on stroke in patients with isolated systolic hypertension and left ventricular hypertrophy. The LIFE study.</a>	J Clin Hypertens (Greenwich) 2005 Mar;7(3):152-8
26	<a href="#">Prognostic value of a new electrocardiographic method for diagnosis of left ventricular hypertrophy in essential hypertension.</a>	J Am Coll Cardiol 1998 Feb;31(2):383-90
27	<a href="#">Losartan benefits over atenolol in non-smoking hypertensive patients with left ventricular hypertrophy: the LIFE study.</a>	Blood Press 2004;13(6):376-84
28	<a href="#">Relationship of the electrocardiographic strain pattern to left ventricular structure and function in hypertensive patients: the LIFE study. Losartan Intervention For End point.</a>	J Am Coll Cardiol 2001 Aug;38(2):514-20
29	<a href="#">[The effect of losartan versus atenolol on cardiovascular morbidity and mortality in patients with hypertension and ECG-verified left ventricular hypertrophy in the LIFE-study]</a>	Ugeskr Laeger 2003 Jan;165(5):456-9
30	<a href="#">Electrocardiographic strain pattern and prediction of cardiovascular morbidity and mortality in hypertensive patients.</a>	Hypertension 2004 Jul;44(1):48-54
31	<a href="#">Cardiovascular risk reduction in hypertensive black patients with left ventricular hypertrophy: the LIFE study.</a>	J Am Coll Cardiol 2004 Mar;43(6):1047-55
32	<a href="#">Changes in survival after acquired immunodeficiency syndrome (AIDS): 1984-1991.</a>	Am J Epidemiol 1993 Dec;138(11):962-64
33	<a href="#">Body mass index and mortality from cardiovascular disease among Japanese men and women: the JACC study.</a>	Stroke 2005 Jul;36(7):1377-82
34	<a href="#">Improved cardiovascular risk stratification by a simple ECG index in hypertension.</a>	Am J Hypertens 2003 Aug;16(8):646-52
35	<a href="#">Cost effectiveness of losartan in patients with hypertension and LVH: an economic evaluation for Sweden of the LIFE trial.</a>	J Hypertens 2005 Jul;23(7):1425-31
36	<a href="#">The prognostic characteristics of hypertensive left ventricular hypertrophy in a population with low prevalence of hypertension and low plasma cholesterol.</a>	Chin Med Sci J 1993 Dec;8(4):197-202
37	<a href="#">Stroke reduction in hypertensive adults with cardiac hypertrophy randomized to losartan versus atenolol: the Losartan Intervention For Endpoint reduction in hypertension study.</a>	Hypertension 2005 Jan;45(1):46-52
38	<a href="#">Long-term plasma catecholamines in patients with hypertension and left ventricular hypertrophy treated with losartan or atenolol: ICARUS, a LIFE substudy.</a>	J Hum Hypertens 2004 Jun;18(6):375-80
39	<a href="#">The impact of serum uric acid on cardiovascular outcomes in the LIFE study.</a>	Kidney Int 2004 Mar;65(3):1041-9
40	<a href="#">[Treatment of hypertension in patients with left ventricular hypertrophy]</a>	Tidskr Nor Laegeforen 2004 Mar;124(6):788-91
41	<a href="#">Diabetes mellitus, impaired glucose tolerance, and hyperinsulinemia in an elderly population. The Rotterdam Study.</a>	Am J Epidemiol 1997 Jan;145(1):24-32
42	<a href="#">The ischemic electrocardiogram: a harbinger for ischemic heart disease independent of the blood pressure level. The Copenhagen City Heart Study.</a>	Eur J Epidemiol 2005;20(4):301-9
43	<a href="#">Body weight change, all-cause mortality, and cause-specific mortality in the Multiple Risk Factor Intervention Trial.</a>	Ann Intern Med 1993 Oct;119(7 Pt 2):749-57
44	<a href="#">Increased prevalence of left ventricular hypertrophy in hypertensive women with type 2 diabetes mellitus.</a>	Cardiovasc Diabetol 2003 Nov;2(0):14
45	<a href="#">Risk factors for the development of type II diabetes among men enrolled in the usual care group of the Multiple Risk Factor Intervention Trial.</a>	Diabetes Care 1993 Oct;16(10):1331-9
46	<a href="#">Angiotensin II receptor blockade reduces new-onset atrial fibrillation and subsequent stroke compared to atenolol: the Losartan Intervention For End Point Reduction in Hypertension (LIFE) study.</a>	J Am Coll Cardiol 2005 Mar;45(5):712-9
47	<a href="#">Hypertension as a risk factor for cardiovascular morbidity and mortality in an elderly German population: the prospective STEPHY II study. Starnberg Study on Epidemiology of Parkinsonism and Hypertension in the Elderly.</a>	Eur Heart J 1999 Dec;20(23):1752-6
48	<a href="#">Impact of atrial fibrillation on the risk of death: the Framingham Heart Study.</a>	Circulation 1998 Sep;98(10):946-52
49	<a href="#">Left ventricular hypertrophy as a predictor of coronary heart disease mortality and the effect of hypertension.</a>	Am Heart J 2000 Dec;140(6):848-56
50	<a href="#">Echocardiographic and electrocardiographic diagnoses of left ventricular hypertrophy predict mortality independently of each other in a population of elderly men.</a>	Circulation 2001 May;103(19):2346-51

図 1 4 q 疫 学(09) 2 6 ~ 5 0 位

その他(10) (選択的 COX-2 阻害薬)

	Title	Journal
1	<a href="#">Comparison of lumiracoxib with naproxen and ibuprofen in the Therapeutic Arthritis Research and Gastrointestinal Event Trial (TARGET), reduction in ulcer complications: randomised controlled trial</a>	Lancet 2004 Aug 21-27;364(9435):665-74
2	<a href="#">Cardiovascular events associated with rofecoxib in a colorectal adenoma chemoprevention trial</a>	N Engl J Med 2005 Mar;352(11):1092-102
3	<a href="#">Risk of cardiovascular events and rofecoxib: cumulative meta-analysis</a>	Lancet 2004 Dec 4-10;364(9450):2021-9
4	<a href="#">Cardiovascular risk associated with celecoxib in a clinical trial for colorectal adenoma prevention</a>	N Engl J Med 2005 Mar;352(11):1071-80
5	<a href="#">Comparison of lumiracoxib with naproxen and ibuprofen in the Therapeutic Arthritis Research and Gastrointestinal Event Trial (TARGET), cardiovascular outcomes: randomised controlled trial</a>	Lancet 2004 Aug 21-27;364(9435):675-84
6	<a href="#">Risk of cardiovascular events associated with selective COX-2 inhibitors</a>	JAMA 2001 Aug 22-29;286(8):954-9
7	<a href="#">Complications of the COX-2 inhibitors parecoxib and valdecoxib after cardiac surgery</a>	N Engl J Med 2005 Mar;352(11):1081-91
8	<a href="#">Cardiovascular thrombotic events in arthritis trials of the cyclooxygenase-2 inhibitor celecoxib</a>	Am J Cardiol 2003 Aug;92(4):411-8
9	<a href="#">Comparison of upper gastrointestinal toxicity of rofecoxib and naproxen in patients with rheumatoid arthritis. VIGOR Study Group</a>	N Engl J Med 2000 Nov;343(21):1520-8, 2 p following 1528
10	<a href="#">Therapeutic arthritis research and gastrointestinal event trial of lumiracoxib - study design and patient demographics</a>	Aliment Pharmacol Ther 2004 Jul;20(1):51-63
11	<a href="#">Cardiovascular thrombotic events in controlled, clinical trials of rofecoxib</a>	Circulation 2001 Nov;104(19):2280-8
12	<a href="#">Selective cyclooxygenase-2 inhibition and cardiovascular effects: an observational study of a Medicaid population</a>	Arch Intern Med 2005 Jan;165(2):181-6
13	<a href="#">Gastrointestinal tolerability and effectiveness of rofecoxib versus naproxen in the treatment of osteoarthritis: a randomized, controlled trial</a>	Ann Intern Med 2003 Oct;139(7):539-46
14	<a href="#">Rofecoxib for rheumatoid arthritis</a>	Cochrane Database Syst Rev 2005;(1);CD003685
15	<a href="#">Risk of myocardial infarction in patients taking cyclo-oxygenase-2 inhibitors or conventional non-steroidal anti-inflammatory drugs: population based nested case-control analysis</a>	BMJ 2005 Jun;330(7504):1366
16	<a href="#">Rofecoxib for osteoarthritis</a>	Cochrane Database Syst Rev 2005;(1);CD005115
17	<a href="#">A comparison of reported gastrointestinal and thromboembolic events between rofecoxib and celecoxib using observational data</a>	Drug Saf 2005;28(9):803-16
18	<a href="#">Comparison of thromboembolic events in patients treated with celecoxib, a cyclooxygenase-2 specific inhibitor, versus ibuprofen or diclofenac</a>	Am J Cardiol 2002 Feb;89(4):425-30
19	<a href="#">Rofecoxib for the treatment of rheumatoid arthritis</a>	Cochrane Database Syst Rev 2002;(3);CD003685
20	<a href="#">Incidence of thrombotic cardiovascular events in patients taking celecoxib compared with those taking rofecoxib: interim results from the New Zealand Intensive Medicines Monitoring Programme</a>	Drug Saf 2005;28(5):435-42
21	<a href="#">Effect of selective cyclooxygenase 2 inhibitors and naproxen on short-term risk of acute myocardial infarction in the elderly</a>	Arch Intern Med 2003 Feb;163(4):481-6
22	<a href="#">A randomized trial of low-dose aspirin in the primary prevention of cardiovascular disease in women</a>	N Engl J Med 2005 Mar;352(13):1293-304
23	<a href="#">The gastrointestinal safety of the COX-2 selective inhibitor etoricoxib assessed by both endoscopy and analysis of upper gastrointestinal events</a>	Am J Gastroenterol 2003 Aug;98(8):1725-33
24	<a href="#">The gastrointestinal safety of the COX-2 selective inhibitor etoricoxib assessed by both endoscopy and analysis of upper gastrointestinal events</a>	N Engl J Med 2003 Jan;342(2):145-53
25	<a href="#">Vitamin E supplementation and cardiovascular events in high-risk patients. The Heart Outcomes Prevention Evaluation Study Investigators</a>	N Engl J Med 2000 Jan;342(3):154-60

図 1 4 r その他(10) (選択的 COX-2 阻害薬) 1 ~ 2 5 位

26	<a href="#">Patients exposed to rofecoxib and celecoxib have different odds of nonfatal myocardial infarction.</a>	Ann Intern Med 2005 Feb;142(3):157-64
27	<a href="#">Incidence of gastroduodenal ulcers in patients with rheumatoid arthritis after 12 weeks of rofecoxib, naproxen, or placebo: a multicentre, randomised, double blind study.</a>	Gut 2003 Jun;52(6):820-6
28	<a href="#">Effects of celecoxib, rofecoxib, and naproxen on the cardiovascular system: a meta-analysis of randomised controlled trials.</a>	Lancet 2003 Sep;362(9386):789-97
29	<a href="#">Single dose oral rofecoxib for postoperative pain.</a>	Cochrane Database Syst Rev 2005;(1):CD004604
30	<a href="#">Efficacy and safety of low-dose aspirin in polycythemia vera.</a>	N Engl J Med 2004 Jan;350(2):114-24
31	<a href="#">Serious lower gastrointestinal clinical events with nonselective NSAID or coxib use.</a>	N Engl J Med 2004 Nov;351(20):2088-98
32	<a href="#">Final report on the aspirin component of the ongoing Physicians' Health Study. Steering Committee of the Physicians' Health Study Research Group.</a>	N Engl J Med 1989 Jul;321(3):129-36
33	<a href="#">Reduced incidence of gastroduodenal ulcers associated with lumiracoxib compared with ibuprofen in patients with rheumatoid arthritis.</a>	Aliment Pharmacol Ther 2004 Jun;19(11):1189-98
34	<a href="#">Relationship between selective cyclooxygenase-2 inhibitors and acute myocardial infarction in older adults.</a>	Circulation 2004 May;109(17):2068-73
35	<a href="#">Oral ximelagatran for secondary prophylaxis after myocardial infarction: the ESTEEM randomised controlled trial.</a>	Lancet 2003 Sep;362(9386):789-97
36	<a href="#">Risk of acute myocardial infarction and sudden cardiac death in patients treated with cyclo-oxygenase 2 selective and non-selective non-steroidal anti-inflammatory drugs: nested case-control study.</a>	Lancet 2005 Feb 5-11;365(9458):475-81
37	<a href="#">The Effects of cyclooxygenase-2 inhibitors and nonsteroidal anti-inflammatory therapy on 24-hour blood pressure in patients with hypertension, osteoarthritis, and type 2 diabetes mellitus.</a>	Arch Intern Med 2005 Jan;165(2):161-8
38	<a href="#">Serious lower gastrointestinal clinical events with nonselective NSAID or coxib use.</a>	Gastroenterology 2003 Feb;124(2):288-92
39	<a href="#">Rofecoxib for the treatment of rheumatoid arthritis.</a>	Cochrane Database Syst Rev 2002;(2):CD003685
40	<a href="#">The upper gastrointestinal safety of rofecoxib vs. NSAIDs: an updated combined analysis.</a>	Curr Med Res Opin 2004 Oct;20(10):1539-48
41	<a href="#">Atorvastatin in patients with type 2 diabetes mellitus undergoing hemodialysis.</a>	N Engl J Med 2005 Jul;353(3):238-48
42	<a href="#">Nonsteroidal anti-inflammatory drugs and aspirin for the prevention of colorectal adenomas and cancer: a systematic review.</a>	Dis Colon Rectum 2004 May;47(5):665-73
43	<a href="#">Cyclo-oxygenase-2 inhibitors versus non-selective non-steroidal anti-inflammatory drugs and congestive heart failure outcomes in elderly patients: a population-based cohort study.</a>	Lancet 2004 May;363(9423):1751-6
44	<a href="#">Adverse events associated with rofecoxib therapy: results of a large study in community-derived osteoarthritic patients.</a>	Drug Saf 2003;26(1):49-54
45	<a href="#">Valsartan, captopril, or both in myocardial infarction complicated by heart failure, left ventricular dysfunction, or both.</a>	N Engl J Med 2003 Nov;349(20):1893-906
46	<a href="#">Effects of celecoxib, rofecoxib, and naproxen on the cardiovascular system: a meta-analysis of randomised controlled trials.</a>	Lancet 2003 Sep;362(9386):789-97
47	<a href="#">Gastrointestinal tolerability of the selective cyclooxygenase-2 (COX-2) inhibitor rofecoxib compared with nonselective COX-1 and COX-2 inhibitors in osteoarthritis.</a>	Arch Intern Med 2000 Oct;160(19):2998-3003
48	<a href="#">The effectiveness of five strategies for the prevention of gastrointestinal toxicity induced by non-steroidal anti-inflammatory drugs: systematic review.</a>	BMJ 2004 Oct;329(7472):948
49	<a href="#">Effects of celecoxib, rofecoxib, and naproxen on the cardiovascular system: a meta-analysis of randomised controlled trials.</a>	Lancet 2003 Sep;362(9386):789-97
50	<a href="#">The cyclooxygenase-2-selective inhibitors rofecoxib and celecoxib prevent colorectal neoplasia occurrence and recurrence.</a>	Gastroenterology 2003 Aug;125(2):404-12

図 1 4 s その他(10) (選択的 COX-2 阻害薬) 26 ~ 50 位

表1 虚血性心疾患の教師データを細分類したことの効果。

	薬 (58)	*	ステント (22)	*	手術 (5)	*
1	A clinical trial comparing primary coronary angioplasty with tissue plasminogen activator for acute myocardial infarction. The Global Use of Strategies to Open Occluded Coronary Arteries in Acute Coronary Syndromes (GUSTO IIb) Angioplasty Substudy Investigators	10	Coronary-artery stenting compared with balloon angioplasty for restenosis after initial balloon angioplasty. Restenosis Stent Study Group.	21	A randomized study of coronary angioplasty compared with bypass surgery in patients with symptomatic multivessel coronary disease. German Angioplasty Bypass Surgery Investigation (GABI)	-
2	Inhibition of platelet glycoprotein IIb/IIIa with eptifibatid in patients with acute coronary syndromes. The PURSUIT Trial Investigators. Platelet Glycoprotein IIb/IIIa in Unstable Angina: Receptor Suppression Using Integrilin Therapy.	30	Stent placement compared with balloon angioplasty for small coronary arteries: in-hospital and 6-month clinical and angiographic results.	107	A randomized trial comparing coronary angioplasty with coronary bypass surgery. Emory Angioplasty versus Surgery Trial (EAST)	100
3	Effect of nicorandil on coronary events in patients with stable angina: the Impact Of Nicorandil in Angina (IONA) randomised trial.	48	Randomized comparison of coronary stent implantation and balloon angioplasty in the treatment of de novo coronary artery lesions (START): a four-year follow-up.	7	A multi-centre randomised controlled trial of minimally invasive direct coronary bypass grafting versus percutaneous transluminal coronary angioplasty with stenting for proximal stenosis of the left anterior descending coronary artery.	-
4	Long-term benefit of primary angioplasty as compared with thrombolytic therapy for acute myocardial infarction.	17	Latin American randomized trial of balloon angioplasty vs coronary stenting for small vessels (LASMAL): immediate and long-term results.	13	Comparison of coronary bypass surgery with angioplasty in patients with multivessel disease. The Bypass Angioplasty Revascularization Investigation (BARI)	-

					Investigators.	
5	Effects of pretreatment with clopidogrel and aspirin followed by long-term therapy in patients undergoing percutaneous coronary intervention: the PCI-CURE study.	2 5	A randomized trial comparing stenting with balloon angioplasty in small vessels in patients with symptomatic coronary artery disease. ISAR-SMART Study Investigators. Intracoronary Stenting or Angioplasty for Restenosis Reduction in Small Arteries.	3	Three-year outcome after coronary stenting versus bypass surgery for the treatment of multivessel disease.	-

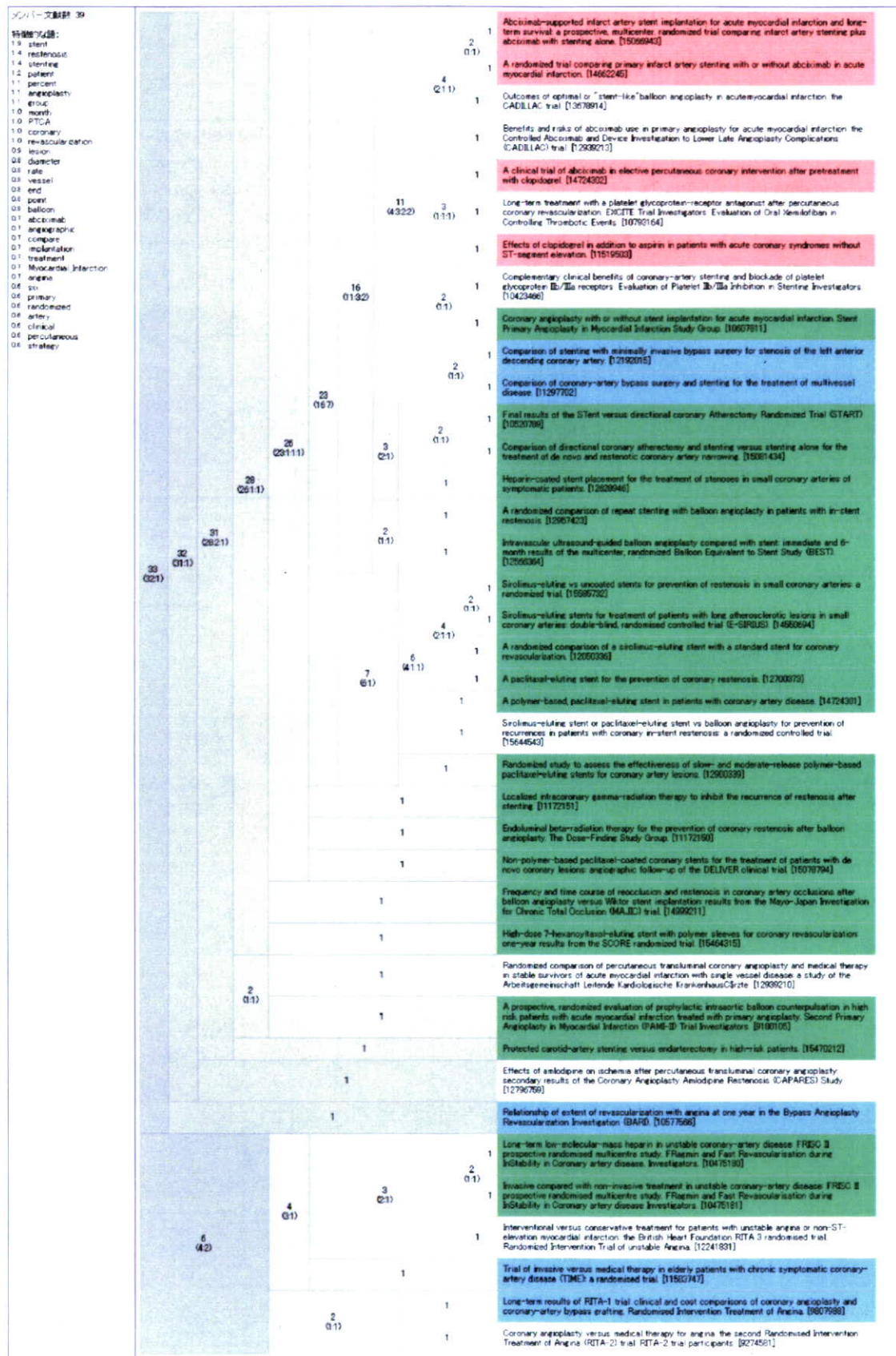


図 15 虚血性心疾患教師データのクラスタリング結果 (a) 第1クラス

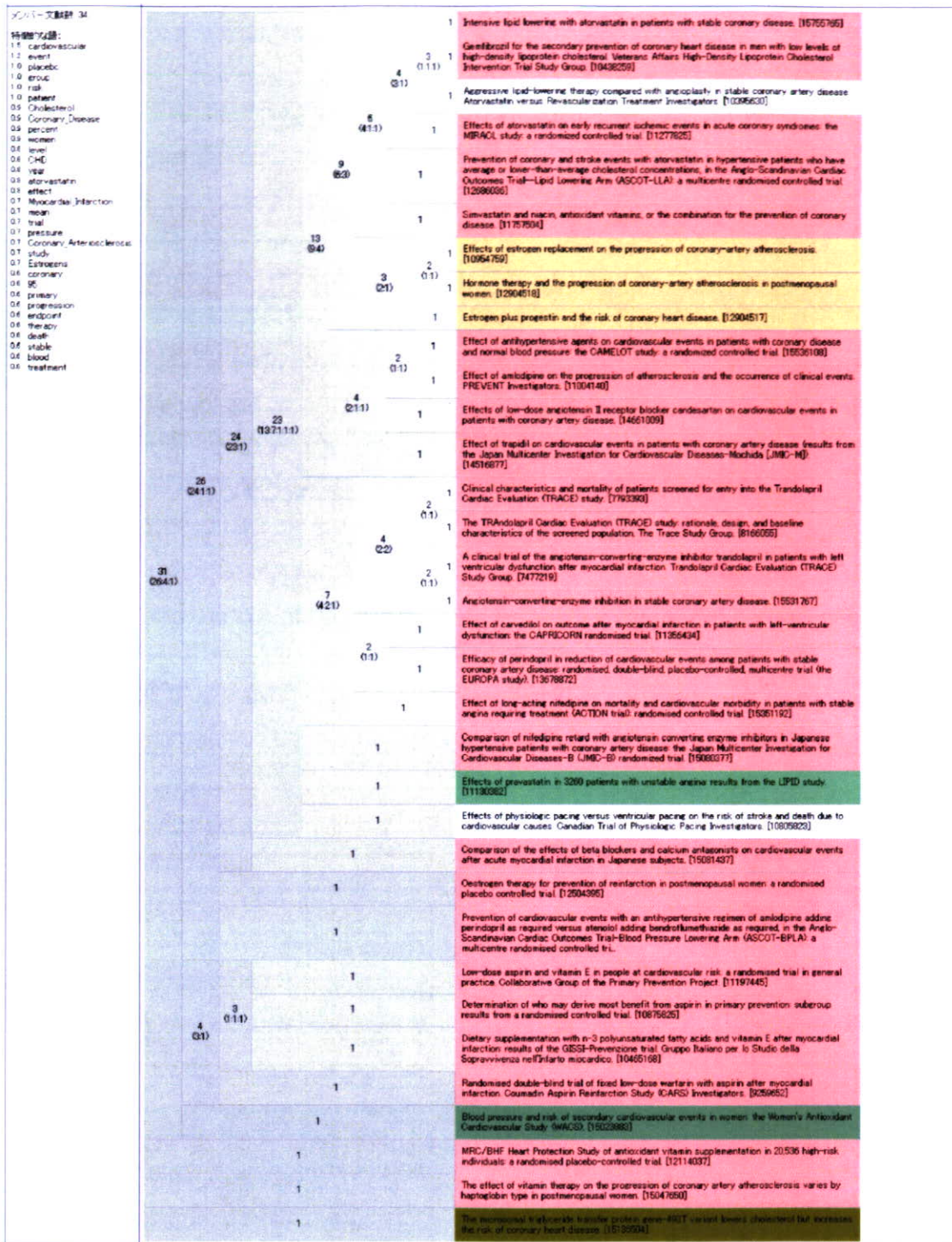


図15 (b) 第2クラス

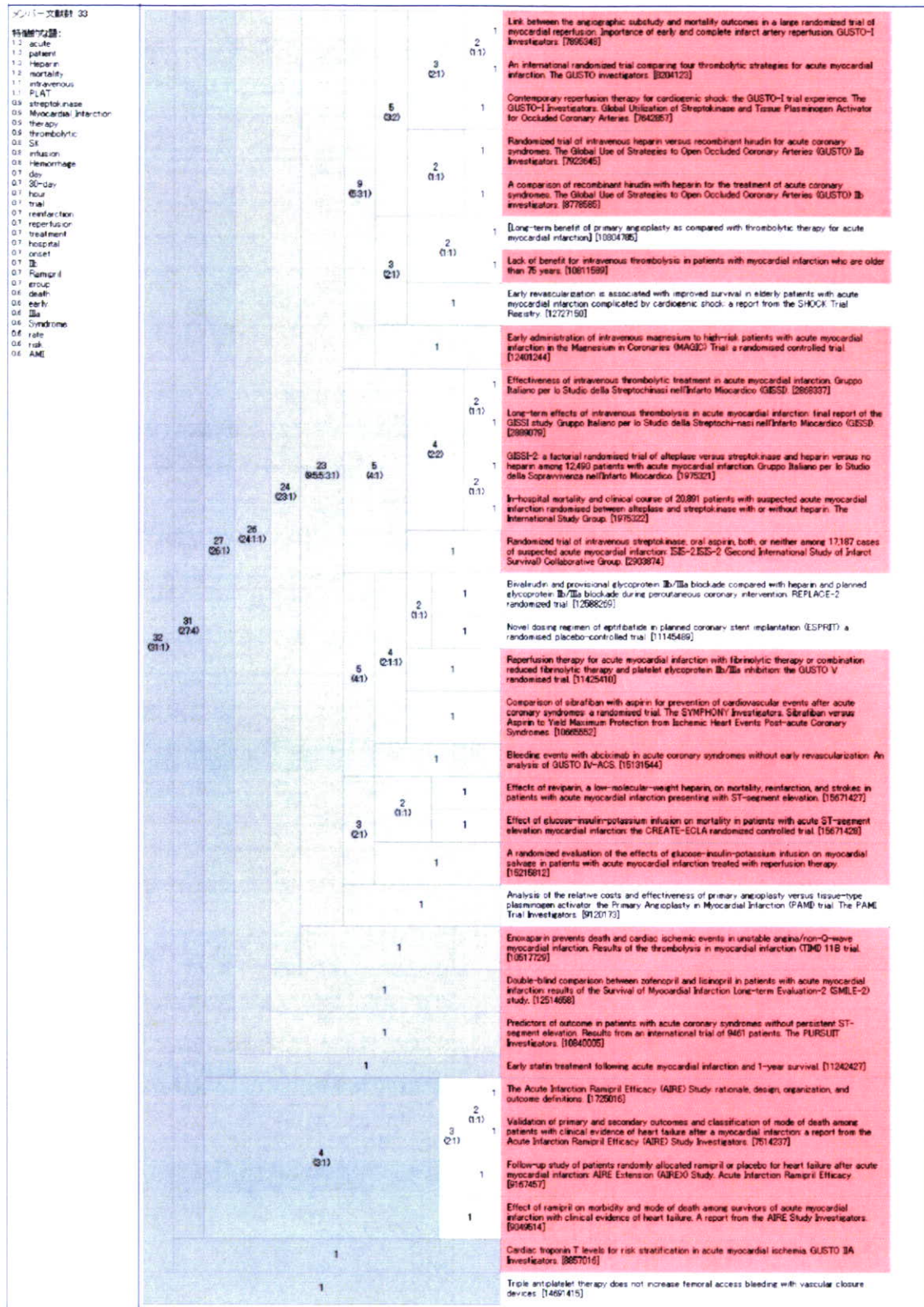


図15 (c) 第3クラス



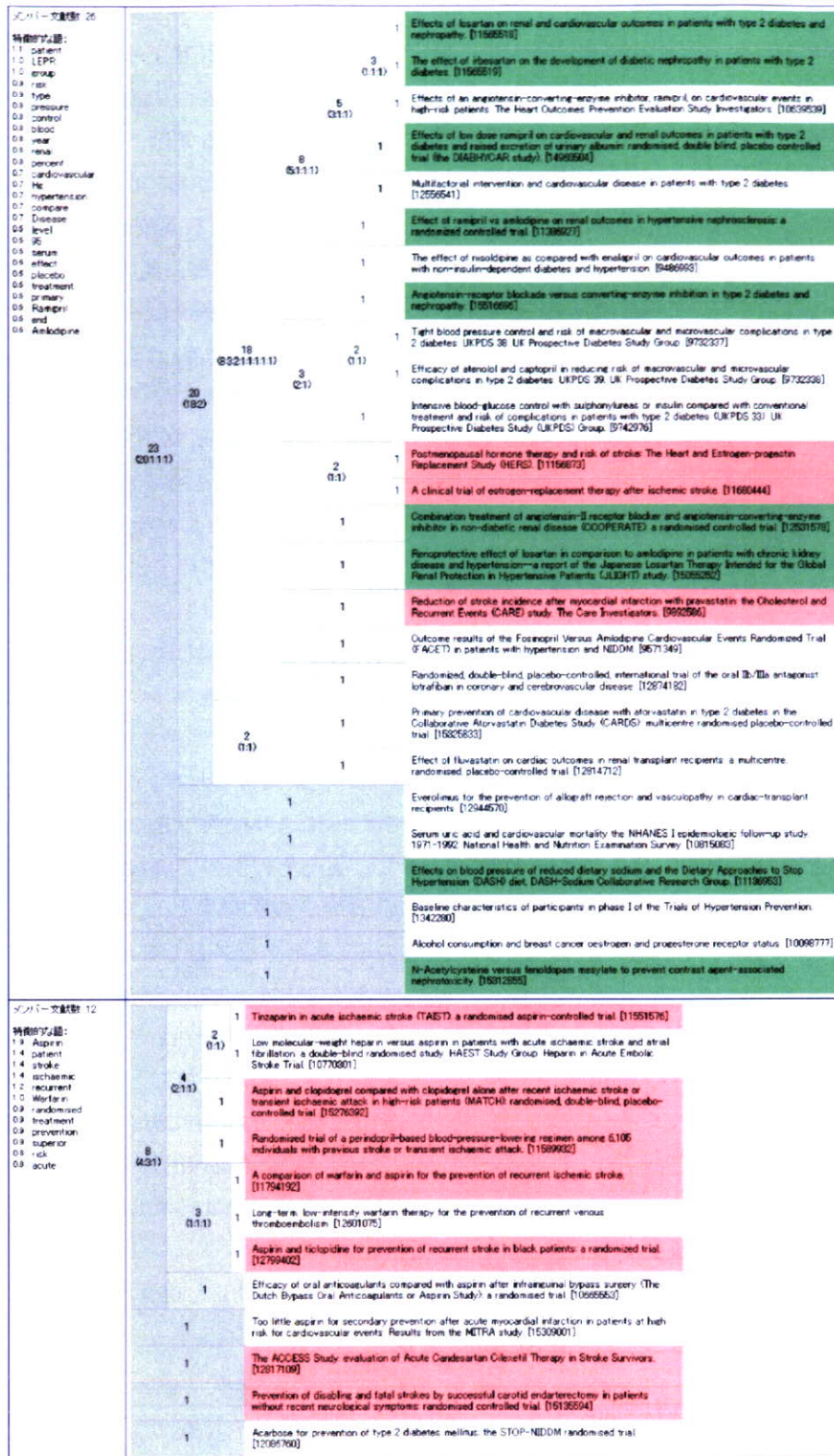


図 1 6 (糖尿病, 脳卒中, 複合領域ほか)  
 教師データのクラスタリング結果  
 緑: 脳 ピンク: 腎

### 第三年度

#### 連想検索システムを用いた薬剤相互作用検索システムの実装

薬剤相互作用検索システムはWeb上で検索できるインターフェースとして実装した(図17)。

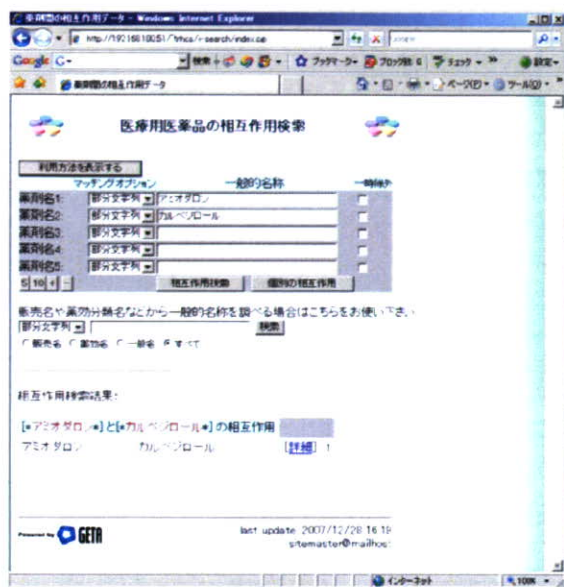


図 17

このシステムを用いて薬物の相互作用の検索テストを行い、通常知られている相互作用をどの程度検索してこられるかを測定した。

#### チトクロームP450:CYP2D6

基質となる薬剤	誘導する薬剤		
	アミオダロン	シメチジン	ジフェンヒドラミン
アミトリプチン	×	○	×
カルベジロール	○	○	×
クロルフェニラミン	×	×	×
コデイン	×	×	×
イミプラミン	×	○	×
メトプロロール	○	○	○
オキシコドン	×	×	×
フレカイニド	○	○	×

#### チトクロームP450:CYP2C9

基質となる薬剤	誘導する薬剤		阻害する薬剤	
	リファンピシン	アミオダロン	フルバスタチン	ミコナゾール
フェニトイン	○	○	×	○
トルブタミド	×	×	×	○
ワルファリン	○	○	○	○

#### チトクロームP450:CYP3A

基質となる薬剤	誘導する薬剤		
	カルバマゼピン	フェノバルビタール	リファンピシン
シクロスボリン	○	○	○
タクロリムス	○	○	○
エチニルエストラジオール	○	○	○
塩酸アミトリプチン	○	△(バルビツール酸誘導体)	○
エリスロマイシン	○、ただし血中濃度上昇	×	△(フルバスタチン、シシロマイシン、クラリスロマイシンが出てくる)
フェロジピン	○	×	○
ニフェジピン	○	△(フェロジピン、アラニジピン、アゼルニジピンで出てくる)	○
ペラミビル	○、ただし血中濃度上昇	○	○
インジナビル	○	○	○
サキナビル	○	○	○
リトナビル	○	○	○
ロサルタン	×	△(バルビツール酸誘導体、起立性低血圧が増強される)	×
ロバスタチン	×	×	△(フルバスタチン、シンバスタチン、アトルバスタチン)
シンバスタチン	×	×	○
メチルプレドニゾロン	○(プレドニゾロンで)	×	○
ミダゾラム	○	△(バルビツール酸誘導体、作用が増強される)	○
シルденаフィル	×	×	○

対象とした薬剤代謝酵素は CYP3A、CYP2D6、CYP2C9 とした。

結果を下の表 3 つに示すが、各酵素には、その酵素が代謝する薬剤、その酵素を誘導し、代謝される薬剤の効果を低下させる薬剤、酵素を阻害し、代謝される薬剤の効果を上昇させる薬剤が存在する(誘導、阻害する薬剤が存在しない場合もある)。例えば、CYP3A により代謝される薬剤として塩酸アミオダロン、硫酸キニジン、ジソピラミド

エルゴタミン製剤、ストレプトグラミン系抗生物質、CYP3A4 活性を誘導する薬剤としてリファンピシン、カルバマゼピン、フェノバルビタールが知られている。

上記 3 酵素に関して、これまで文献的に報告されている結果を本システムを用いて検索した結果を表 1~3 に示す。

○は、従来報告されている相互作用が本検索システムにより検索できた場合、△は検索対象とした薬剤そのものではなかったものの、同系統の薬剤が検索結果として引っかかってきたものや、薬剤クラスとして結果が返ってきたものであることを示す。×は本検索システムが備えている曖昧検索を用いても一切検索結果として返ってこなかったことを示す。薬剤代謝酵素を介した相互作用はあくまでも理論的なものであり、実際に臨床的に有意な相互作用を引き起こすかどうかは必ずしも明らかではない。例

えば、ジフェンヒドラミンは理論上は CYP2D6 を誘導する作用を示し、基質となるアミトリプチン、カルベジロー

ル、イミプラミンなどの血中濃度を低下させるはずであるが、本検索システムではそうした相互作用は検出されず、また実際に添付文書を吟味しても相互作用の記載は認められなかった。

#### 心臓カテーテルレポートシステムからのデータ抽出ツールの改良

改良されたツールを用いて心臓を養う冠動脈が慢性的に閉塞した病変(CTO 病変)に対する治療方法の選択およびその治療成績をまとめた。結果の詳細は参考資料を参照のこと。CTO 病変をより具体的に定義すると、冠動脈が閉塞してから一ヶ月以上経過した病変であり、これまでステント植込による初期治療には成功しても、晩期に高率に再狭窄することが臨床問題になっていた。近年、再狭窄を予防するために、ステントにパクリタクセルやシロリムスなどの再狭窄を予防する薬剤を予め埋め込み、ステント留置後に徐々に溶出して再狭窄を予防するものが市販されるようになった。

東大病院においては術前であったり、服薬を十分遵守できなかつたりする症例に対してやむを得ずに CTO 病変に対する治療として従来型ステントを用いざるを得ない症例が少数例いたが、これらはその後の調査で全症例再狭窄を起こしていたことが分かった。それに対して薬剤溶出ステントを用いた場合は、晩期の再狭窄率は 27.8% であり、大幅に少なかった。この調査結果からも分かるようにこうした新しいデバイスを用いた場合の実際の治療成績を知ることは医療の質評価を行う上で重要であり、本システムの有用性を示すものであった。

#### **D. 考察**

初年度において構築し臨床現場に導入したカテーテルレポートシステムは虚血性心疾患検査・治療の詳細なデータを収集する上で有用なツールであり、第三年度における抽出ツールの改良により、使用デバイスによる治療成績の差を短期間に抽出することが可能であった。ま

た薬剤相互作用検索システムや既存の文献を対象にした臨床知の抽出も有用であることが分かった。

日本の医療現場において、IT 技術の導入は主として医事会計(レセプト)システムから始まり、その後、処方や検査の指示を行い、画像情報や検査結果情報をオンラインで共有して閲覧していくことの可能ないわゆるオーダリングシステムへと進化し、さらに診療録そのものを全て電子化した形で記録する電子カルテシステムへと発展を遂げてきている。

しかし、基本的な発想が医事会計を間違いなく行うためのシステム、オーダの取り漏れがないように補助するためのシステム、ということであるために臨床的に有用な知見の抽出が難しい。具体的には、保険請求のために必要な病名(保険病名)は必ずしも臨床的に重要な順位付けとは関係が無く、保険病名をもとにした臨床データ解析にはかなり大きな制約がともなう。

こうした問題意識から我々は病院の医療情報システムとは別個に循環器内科分野における臨床情報システムを構築してきた。第三年度の研究において従来のツールに改良を加えることにより、データベースから臨床上有用な知見を抽出することができた。

#### **E. 結論**

本研究においては循環器診療支援データベースシステムの維持・改良、虚血性心疾患診断・治療支援システムの構築、連想検索技術を応用した既存文献からの臨床知の抽出、薬剤相互作用検索システムの構築を行い、臨床現場において用いてきた。これらにより、治療デバイスによる治療成績の差を比較的短期間に抽出し、その知見を臨床現場に返すことにより医療の質向上に役立てることが可能であることが分かった。一方、薬剤相互作用検索システムを構築し、その有用性を検証したところ、参照データとして用いた薬剤添付文書に形式・内容上

改善すべき点があることが分かった。これまで、臨床の実態を IT を活用して観察し分析した研究は他にほとんどなく、本研究の成果は非常に貴重であると考えられると共に今後も同様の研究を継続していくことが重要であると考えられる。

#### **F.健康危険情報**

特記すべき事無し

#### **G.研究発表**

##### **1.論文発表**

特になし

##### **2.学会発表**

特になし

#### **H.知的財産権の出願・登録状況**

##### **1.特許取得**

特になし

##### **2.実用新案登録**

特になし

##### **3.その他**

特になし