ABSTRACTS

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Lifestyle, diabetes, and cardiovascular risk factors 10 years after bariatric surgery

Sjöström L, Lindroos A-K, Peltonen M, and The Swedish Obese Subjects Study Scientific Group. N Engl J Med 2004;351:2683-93.

Conclusion: Bariatric surgery, when compared with conventional obesity therapy, provides better long-term weight loss, improved lifestyle, and amelioration of cardiovascular risk factors, with the exception of hypercholesterolemia.

Summary: The Swedish Obese Subjects Study is a prospective investigation involving obese subjects who underwent bariatric surgery or conventional treatment for obesity. This report documents follow-up data for subjects (mean age, 48 years; mean body mass index, 41 kg/m^2) who were enrolled in the study for at least 2 years (4047 subjects) or 10 years (1703 subjects). The follow-up rate for laboratory examinations was 86.6% at 2 years and 74.5% at 10 years.

After 2 years of follow-up, weight increased 0.1% in the control group and decreased 23.4% in the surgery group ($P < .001$). After 10 years, weight had increased by 1.6% in the control group and had decreased by 16.1% in the surgery group ($P < .001$). There were proportionally more physically active subjects in the surgery group than in the control group throughout the observation period. Two- to 10-year recovery rates from hypertriglyceridemia, low levels of high-density lipoprotein cholesterol, diabetes, hypertension, and hyperuricemia were more favorable in the surgery than the control group. There were no differences in recovery from hypercholesterolemia in the control and surgery groups. The surgery group had lower 2- and 10-year incidence rates of diabetes, hypertriglyceridemia, and hyperuricemia than the control group. There were no differences between the groups in the incidence of hypercholesterolemia and hypertension.

Comment: This was not a randomized study. The data, however, strongly implicate bariatric surgery as an effective means of improving cardiovascular risk factors in the morbidly obese. The study does not tell us whether progression of established vascular disease in the morbidly obese can be slowed by bariatric surgery. We are not currently at the point where we can recommend bariatric surgery as a treatment to slow progression of peripheral vascular disease. However, in patients with established cardiovascular risk factors who are morbidly obese, bariatric surgery can be recommended to diminish these risk factors and improve lifestyle.

Subintimal angioplasty in the treatment of patients with intermittent claudication: Long-term results

Florenes T, Bay D, Sandbaek G, et al. Eur J Vasc Endovasc Surg 2004;28: 645-50.

Conclusion: Subintimal angioplasty should be the primary treatment for patients with intermittent claudication when medical treatment alone has been unsatisfactory.

Summary: The authors report the results of subintimal angioplasty used for treatment of patients with intermittent claudication. The authors performed 116 subintimal angioplasties in 104 patients from February 1997 to January 2000. The authors calculated primary assisted patency rates for successful angioplasties, as well as calculated primary assisted patency rates, on an intention-to-treat basis. Univariant and multivariant Cox regression analysis was used to evaluate correlations of patency with comorbidities, occlusion length, and runoff.

Technical success was achieved in 87% (n = 101) of cases. There was no early mortality. On an attention-to-treat basis (116 cases), primary assisted patency at 6, 12, 36, and 60 months was 69%, 62%, 57%, and 54%, respectively. In successfully recanalized cases (101 cases), primary assisted patency at 6, 12, 36, and 60 months was 79%, 70%, 66%, and 64%. The risk of reocclusion was related to length of occlusion, age, and male sex. Periprocedural complications included seven hematomas, one requiring surgical evacuation, and six perforations that did not require intervention.

Comment: The patency results in this study are reasonable, but overall the paper is not all that helpful. We already know that subintimal angioplasty can be successful. The goal of treatment in patients with intermittent claudication, however, is improvement in walking and quality of life. The authors do not even present hemodynamic data, much less data regarding walking and quality of life. In a prospective study of treatment for intermittent claudication, more functional data, and not just simple patency analysis, should be included.

Risk of acute myocardial infarction and sudden cardiac death in patients treated with cyclo-oxygenase 2 selective and non-selective non-steroidal inflammatory drugs: Nested case-control study

Graham DJ, Campen D, Hui R, et al. Lancet Online Publication, January 25, 2005

Conclusion: Compared with celecoxib, rofecoxib increases the risk of serious coronary heart disease. Naproxen does not offer a protective effect against coronary heart disease.

Summary: The Vioxx Gastrointestinal Outcomes Research Trial (VIGOR) raised questions about the cardiovascular risk of COX-2–selective drugs. In this trial, there was a fivefold difference in the incidence of acute myocardial infarction in patients treated with rofecoxib 50 mg/d and naproxen 1000 mg/d. There was no placebo group in this trial; therefore, findings could suggest adverse effects of coxibs in general, an adverse effect of rofecoxib, or a previously unrecognized protective effect of naproxen. The authors sought to establish whether cardiovascular risk was increased with rofecoxib at standard or high doses in comparison to remote nonsteroidal anti-inflammatory drug (NSAID) use or celecoxib. Celecoxib was chosen as a comparison drug to rofecoxib because celecoxib was the most common alternative to rofecoxib.

This was a nested case-control study. Data were derived from Kaiser Permanente in California. The authors assembled a cohort of all patients aged 18 to 84 years treated with NSAIDs between January 1, 1999, and December 31, 2001. Cases of serious coronary heart disease (defined as acute myocardial infarction and cardiac death) were risk-set–matched for age, sex, and health plan region. There were four controls for each case. The authors compared current exposure to COX-2–selective and –nonselective NSAIDS and to remote exposure to any NSAID. Rofecoxib was also compared with celecoxib.

There were 2,302,029 person-years of follow-up. There were 8143 cases of serious coronary heart disease, 27.1% (n = 2210) of which were fatal. Multivariant adjusted odds ratios vs celecoxib were as follows: for rofecoxib (any dose), 1.59 (95% CI, 1.1-2.32; $P = .015$); for rofecoxib 25 mg/d or less, 1.47 (95% CI, 0.99-2.17; $P = .054$); and for rofecoxib greater than 25 mg/d, 3.58 (95% CI, 1.27-10.11; $P = .016$). For naproxen vs past NSAID use, the adjusted odds ratio was 1.14 (95% CI, 1.00-1.30; $P = .05$).

Comment: Parts of this article were first posted on the US Food and Drug Administration (FDA) Web site on November 2, 2004. At that point, the document was considered preliminary and was a source of great controversy within the FDA. It is important to recognize that the current document represents the opinion of the authors and not necessarily that of the FDA and that the FDA did not participate in the study design, data collection, analysis, or writing of this report. This study, however, obviously has enormous implications for the entire class of COX-2 inhibitors and the mechanisms of oversight used by the FDA.

Randomized clinical trial of intraoperative autotransfusion in surgery for abdominal aortic aneurysm

Mercer KG, Spark JI, Berridge DC, et al. Br J Surg 2004;91:1443-8.

Conclusion: Autotransfusion effectively reduces the need for homologous blood transfusion (HBT) during repair of abdominal aortic aneurysm (AAA). Use of autotransfusion was associated with a reduced incidence of both the systemic inflammatory response syndrome (SIRS) and postoperative infectious complications.

Summary: This was a randomized, single-center clinical trial of intraoperative autotransfusion in patients undergoing repair of AAA. There were 40 patients randomized to intraoperative autotransfusion and 41 patients who underwent surgery for AAA with homologous blood transfusion alone. Patients in both groups received, when necessary, HBT to maintain hemoglobin levels >8 g/dL. Comparisons were made among transfusion requirements, the incidence of infection, and the incidence of SIRS between the two groups.

Fewer patients in the intraoperative autotransfusion group required HBT (21 vs 31; $P = .038$). The median blood requirement per patient was two units lower in the patients undergoing intraoperative autotransfusion vs those treated with HBT alone ($P = .012$). There was a higher incidence of SIRS (20 vs 9 patients; $P = .020$) and a higher incidence of chest infection (12 vs 4 patients; $P = .049$) in the HBT-alone group. The risk of SIRS was related to aortic cross-clamp time in the intraoperative autotransfusion group only.

Comment: The author's finding that intraoperative autotransfusion is associated with reduced postoperative infection is consistent with observational studies linking a diminished immunologic response to HBT. The

mechanism of this potential decrease in immunologic competence with HBT is unknown. The observation, however, provides another reason, in addition to those of conserving blood bank resources and diminishing direct bloodborne infections, for use of intraoperative autotransfusion.

Histological correlates of carotid plaque surface morphology on lumen contrast imaging

Lovett JK, Gallagher PJ, Hands LJ, et al. Circulation 2004;110:2190-7.

Conclusion: There are strong associations between detailed histologic analysis and carotid angiographic plaque surface morphology. Surface morphology on carotid angiography is a highly sensitive marker of plaque instability.

Summary: Studies comparing angiographic plaque surface morphology and carotid plaque pathology have been small and unblinded. Most have assessed only the macroscopic appearance of the plaque. The authors performed a large study comparing angiographic surface morphology with detailed histologic analysis of the plaque.

On the basis of conventional selective carotid arteriograms in patients undergoing endarterectomy for severe symptomatic stenosis, carotid plaque surface morphology was classified as irregular, smooth, or ulcerated. There were 128 selective arteriographic studies included in this study. Angiographic assessment was blinded and was compared with 10 histologic features recorded on detailed microscopy of the plaque. These features were recorded by using reproducible semiquantitative scales.

Ulceration on angiography was associated with plaque rupture ($P = .001$), a large lipid core ($P = .005$), intraplaque hemorrhage ($P = .001$), decreased fibrous tissue ($P = .003$), and increased overall instability ($P = .001$). Ulcerated plaques on angiography were more likely than smooth plaques to be ruptured (OR = 15.4, 95% CI = 2.7-87.3, $P < 0.001$), show a large lipid core (OR = 26.7, 95% CI = 2.6-270, $P < 0.001$), or have a large intraplaque hemorrhage (OR = 17.0, 95% CI = 2.0-147, $P = 0.02$).

Comment: This is the largest study to compare plaque histology with angiographic surface morphology. That angiographic features of irregularity and ulceration predict histologic features of unstable plaques suggests that assessment of the plaque surface by contrast studies may be useful in predicting carotid plaque instability.

Clinical lower extremity ischemia: A human model of ischemia tolerance

Badhwar A, Forbes TL, Lovell MB. Can J Surg 2004;47:352-8.

Conclusion: Acute ischemia followed by reperfusion results in less ischemic damage to muscle tissue in patients with chronic lower extremity ischemia in comparison to patients without chronic lower extremity ischemia prior to the acute ischemic insult.

Summary: Ischemic preconditioning has a protective effect against future ischemic injury to muscle tissue. Some ischemia is unavoidable during vascular surgical procedures involving arteries to the lower extremity. The authors sought to determine whether there are different degrees of ischemia/reperfusion injury in patients undergoing vascular surgery for occlusive disease vs aneurysm repair.

The authors studied three groups of patients from a university-affiliated medical center. The first group (n = 6) had chronic lower extremity ischemia and were undergoing femoral distal bypass. Four patients (group 2) underwent aortofemoral bypass for aortoiliac occlusive disease, and seven patients underwent elective open repair of an infrarenal abdominal aortic aneurysm and had no associated occlusive disease (group 3; control group). Three hematologic indicators of skeletal muscle injury (creatine kinase [CK], lactate dehydrogenase [LDH], and myoglobin) were measured immediately prior to induction of surgical ischemia, during surgical ischemia, immediately upon reperfusion, 15 minutes after reperfusion, 1 hour after reperfusion, and during the first, second, and third postoperative days.

Markers of skeletal injury at baseline were similar in all groups. Postreperfusion concentrations of markers of muscle injury were lower in the two groups undergoing operation for occlusive disease than in the aneurysm control group. At day 2, LDH levels were increased approximately 30% in the aneurysm control group compared with the distal bypass and aortoiliac occlusive disease groups ($P < .05$). Myoglobin increased 977% in the aneurysm group but only 160% in the distal bypass group and 528% in the aortobifemoral bypass group ($P < .01$). CK levels were 1432% higher in the aneurysm group, only 111% higher in the distal bypass group, and 120% higher in the aortofemoral occlusive disease group ($P < .05$).

Comment: The author's model is far from perfect. Patients undergoing AAA repair have many more things rendered ischemic during aneurysm repair than just leg muscles. AAA repair involves pelvic ischemia and likely some degree of colon ischemia that does not occur during lower extremity bypass. It is well recognized that patients with chronic lower extremity ischemia tolerate acute occlusion better than patients without chronic occlusive disease. However, this may be due to more extensive collateral development in patients with chronic ischemia rather than ischemic preconditioning of the muscle tissue itself.

Risk of myocardial infarction and stroke after acute infection or vaccination

Smeeth L, Thomas SL, Hall HJ, et al. N Engl J Med 2004;351:2611-8.

Conclusion: Acute infections are associated with a temporary increase in the risk of vascular events.

Summary: It is known that chronic infection may promote atherosclerotic disease. The authors sought to examine whether a vaccination or acute infection increases the short-term risk of cardiovascular events. A case-series method was used to study within-person comparisons of risk of myocardial infarction and stroke after naturally occurring infections and commonly used vaccinations. Data were extracted from the general practice research database of the United Kingdom. This database contains medical records of more than 5 million patients.

The analysis included 19,063 patients with a first stroke who received influenza vaccine and 20,484 persons with a first myocardial infarction. There was no increase in the risk of stroke or myocardial infarction after pneumococcal, tetanus, or influenza vaccine. Both stroke and myocardial infarction were increased after a diagnosis of respiratory tract infection. Risks were highest during the first 3 days (incident ratio for stroke, 3.19; 95% CI, 2.81-3.62; incident rate for myocardial infarction, 4.95; 95% CI, 4.3-5.53.) Risk was also increased after urinary tract infection but was not as pronounced as after upper respiratory tract infection.

Comment: This very large database supports a link between acute infection and vascular events. It now needs to be established whether the risk is due to alterations in red cell activation, dehydration, or perhaps the institution of bed rest with the illness. The authors correctly point out that the associated increased risk of cardiovascular events with infection in two very different organ systems suggests the possibility of an underlying genetic basis for this increased risk.

Different effects of anti-hypertensive regimens based on fosinopril or hydrochlorothiazide with or without lipid lowering by pravastatin on progression of asymptomatic carotid arthrosclerosis. Principal results of PHYLLIS—A randomized double-blind trial

Zanchetti A, Crepaldi G, Bond MG, et al. Stroke 2004;35:2807-12.

Conclusion: Carotid atherosclerosis progression occurs with hydrochlorothiazide, but not with the ACE inhibitor fosinopril. Carotid atherosclerosis can also be prevented by the combination of pravastatin and hydrochlorothiazide.

Summary: Patients with hypertension and hypercholesterolemia are at risk for progression of carotid atherosclerosis. This study reports the result of PHYLLIS (the plaque hypertension lipid-lowering Italian study). The study was designed to test, in hypertensive patients with hypercholesterolemia and asymptomatic atherosclerosis, (1) whether antihypertensive therapy with an ACE inhibitor (fosinopril) was more effective in preventing the progression of carotid atherosclerosis than antihypertensive therapy with hydrochlorothiazide; (2) whether lipid lowering with pravastatin was more effective than placebo when associated with either hydrochlorothiazide or fosinopril; and (3) whether there were additive effects of lipid-lowering therapies and ACE inhibitors on carotid atherosclerosis progression. Patients receiving fosinopril received 20 g/d, those receiving hydrochlorothiazide received 25 mg/d, and the pravastatin dose was 40 mg/d.

There were 508 patients with hypercholesterolemia, hypertension, and asymptomatic carotid stenosis randomized to (A) hydrochlorothiazide, (B) fosinopril, (C) hydrochlorothiazide plus pravastatin, and (D) fosinopril plus pravastatin. Follow-up was for 2.6 years, with the investigators blinded to the drug. There were 13 centers involved. B-mode carotid duplex scans for intima-medial thickness were performed at local centers and read centrally. The primary end point was mean maximal intima-media thickness of the near and far walls of the common carotid arteries and common carotid bifurcations bilaterally (CBM_{max}).

CBM_{max} progressed significantly in group A (hydrochlorothiazide alone) but not in groups B, C, or D (0.010 ± 0.004 mm/y). Sites of CBM_{max} changes in groups B, C, and D were different from those changes in group A, with group A changes concentrated at the bifurcation. Blood pressure reductions were not significantly different between groups, but low-density and total lipoprotein cholesterol decreased by 1 mL/L in groups C and D.

Comment: We are rapidly moving toward a "cocktail" of drugs for patients with atherosclerosis or at risk of atherosclerosis. This study demonstrates that an ACE inhibitor and a statin can inhibit progression of atherosclerosis at the carotid bifurcation. The effect of ACE inhibitors and statins on cerebrovascular clinical events cannot be determined from this study. Nevertheless, this is another bit of support for essentially routine use of a statin, a β-blocker, and now an ACE inhibitor in patients who are at significant risk for progression of atherosclerosis.