Abstracts

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Impact of a High Loading Dose of Atorvastatin on Contrast-Induced Acute Kidney Injury
Quintavalle C, Fiore D, De Micco F, et al. Circulation 2012;126:3008-16.

Conclusion: A single high loading dose of atorvastatin administered ≤24 hours before contrast media (CM) exposure reduces the rate of contrast-induced acute kidney injury (CIAKI). The benefit is only seen in patients at low to medium risk.

Summary: After the administration of intravenous contrast CIAKI occurs in <1% to >50% of patients, depending on risk factors and the patient population studied (McCullough PA, J Am Coll Cardiol 2008;51:1419-28). CM is felt to introduce harmful hemodynamic changes in renal blood flow, leading to hypoxia of the renal medulla and direct toxic effects on renal cells (Tumlin J et al, Am J Cardiol 2006;98:14-20K). CM may also induce apoptotic cell death. Among the pleiotropic effects of statins are their effects on the apoptotic pathway. In the present study, the authors investigated the effects of atorvastatin pretreatment on CIAKI and the effects of atorvastatin pretreatment on CM-mediated modifications of intercellular pathways leading to apoptosis or survival of renal tubular cells. The authors first investigated the in vivo effects of atorvastatin on CIAKI in patients with chronic kidney disease enrolled in the Novel Approaches for Preventing or Limiting Events (NAPLES) II trial. Patients were randomly assigned to an atorvastatin group (80 mg ≤24 hours before CM exposure; n = 202) or to the control group (n = 208). All patients received a high dose of N-acetylcysteine and sodium bicarbonate solution. Second, the authors investigated the in vitro effects of atorvastatin pretreatment on CM-mediated modifications of intercellular pathways potentially leading to apoptosis or survival of renal tubular cells. CIAKI, defined as an increase of 10% of serum cystatin C concentration ≤24 hours of CM exposure, occurred in 9 of 202 patients (4.5%) in the atorvastatin group and in 37 of 208 patients (17.8%) in the control group (odds ratio, 0.22; 95% confidence interval, 0.70-0.69; $P = .005$). The CIAKI rate was lower in the atorvastatin group in diabetic and nondiabetic patients and in patients with moderate chronic kidney disease (estimated glomerular filtration rate, 31-60 mg/min/1.73 m^2). In the in vitro model, pretreatment with atorvastatin, prevented CM-induced renal cell apoptosis and restored survival signals mediated by protein kinase B (AKT) and extracellular signal-regulated kinase (ERK) pathways.

Comment: The concept of adding a single high loading dose of atorvastatin before CM exposure to prevent CIAKI is attractive. The treatment is easy to do and likely very safe. This study suggests still another pleiotropic effect of statin medications, but it appears to be confined only to patients at low to medium risk of CIAKI.

Randomized Clinical Trial of Endovenous Laser Ablation Versus Conventional Surgery for Small Saphenous Varicose Veins
Samuel N, Carradice D, Wallace T, et al. Ann Surg 2012;00:1-8.

Conclusion: Endovenous laser ablation (EVLA) and conventional surgery produce similar improvements in the venous clinical severity scores and quality of life in the treatment of small saphenous varicose veins. EVLA has less periprocedural morbidity, providing faster recovery.

Summary: About 15% of patients with symptomatic varicose veins have isolated saphenopopliteal junction incompetence associated with small saphenous vein reflux (Engelhorn CA et al, J Vasc Surg 2005;41:645-51). Open surgical treatment of saphenopopliteal junction reflux has been the accepted gold standard treatment of small saphenous vein incompetence. However, surgical exploration of the saphenopopliteal junction is considered more technically challenging than that of the saphenofemoral junction. There is a lack of consensus on treatment for saphenopopliteal junction incompetence (Winterborn RJ et al, Eur J Vasc Endovasc Surg 2004;28:400-3). Endovenous procedures have advantages over open striping procedures for treatment of great saphenous vein incompetence with respect to perioperative morbidity. There have been a number of randomized trials in which endovenous ablation techniques have been compared with greater saphenous vein stripping but no such trials for the treatment of saphenopopliteal incompetence. In this particular trial the so-called gold standard of conventional surgery for saphenopopliteal junction incompetence was compared with EVLA in the management of small saphenous vein incompetence. Patients with unilateral primary saphenopopliteal junction incompetence and small saphenous vein reflux were randomized equally in parallel groups receiving EVLA or surgery. Patients were assessed at baseline and at 1, 6, 12, and 52 weeks. Outcomes included successful ablation of axial reflux on duplex imaging, visual analog pain scores, recovery times, complication rates, venous clinical severity scores, and quality of life profiling. A total of 106 patients were recruited and randomized to surgery (n = 53) or EVLA (n = 53). EVLA resulted in a higher ablation of short saphenous vein reflux than surgery (96.2% vs 71.7%; $P < .001$). Postoperative pain was lower after EVLA ($P < .05$). Patients returned to work earlier after EVLA, with quicker return to normal function ($P < .001$). The incidence of minor sensory disturbances was 26.4% with surgery vs 7.5% in the EVLA group ($P = .009$). There were similar improvements in venous clinical severity scores and measures of quality of life.

Comment: The data very much mirror randomized data for the comparison of stripping of the great saphenous vein vs endovenous ablation techniques. Longer-term outcomes are similar but, with less pain and faster recovery using the EVLA techniques. The data here are only presented out to 1 year. Because EVLA seems to be more effective in addressing the underlying pathophysiology of small saphenous vein incompetence, even longer-term data will be needed to ultimately determine whether recurrence rates with EVLA for small saphenous insufficiency will, in fact, be lower than with open surgery.

Low-Dose Aspirin for Preventing Recurrent Venous Thromboembolism
Brighton TA, Eikelboom JW, Mann K, and the ASPIRE Investigators.
N Engl J Med 2012;367:1979-87.

Conclusion: Aspirin did not reduce the rate of recurrence of venous thromboembolism after a first episode of unprovoked venous thromboembolism.

Summary: It is well known that after an episode of unprovoked venous thromboembolism (VTE), patients are at significant risk for recurrent VTE after discontinuation of anticoagulation therapy. Long-term treatment with vitamin K antagonists reduces the risk of recurrent VTE but does not improve survival and is associated with increased risk for bleeding. Low-dose aspirin is inexpensive and simple to administer and clearly effective in the prevention of arterial vascular events. It has been used as primary prevention of VTE in high-risk surgical patients (Antiplatelet Trialists' Collaboration, BMJ 2002;324:71-86). It has also been suggested that aspirin may be effective in preventing recurrence of VTE after an initial event (Becattini C et al, N Engl J Med 2012;366:1959-67). The authors of this study randomly assigned 822 patients who had completed initial anticoagulation therapy after a first episode of unprovoked VTE to receive aspirin at a dose of 100 mg/d or placebo for up to 4 years. Primary outcome was recurrence of VTE. During the median follow-up of 37.2 months, VTE recurred in 73 of 411 patients treated with placebo and in 57 of 411 assigned to aspirin (6.5% per year for placebo vs 4.8% per year for aspirin; hazard risk [HR] with aspirin, 0.74; 95% confidence interval [CI], 0.25-1.05; $P = .09$). Aspirin reduced the rate of two prespecified secondary composite outcomes. The rate of VTE, myocardial infarction, stroke, or cardiovascular death was reduced by 34% (8% per year for placebo vs 5.2% per year with aspirin; HR with aspirin, 0.66; 95% CI, 0.48-0.92; $P = .01$). The rate of VTE, myocardial infarction, stroke, major bleeding, or death from any cause was reduced by 33% (HR 0.67; 95% CI, 0.49-0.91; $P = .01$). There were no differences in the rates of major or clinically relevant nonmajor bleeding episodes (0.6% per year for placebo vs 1.1% per year for aspirin; $P = .22$).

Comment: The authors point out that the ASPIRE trial was not sufficiently powered to show a significant reduction in the primary end point of recurrent VTE. Their data when combined, as prospectively planned, with the WARFASA Study (Becattini C et al, N Engl J Med 2012;366:1959-67) did show a clear aspirin effect. Combined results of the WARFASA and the ASPIRE trial show a highly significant reduction of 32% in recurrent VTE ($P = .007$) and a reduction of 34% in rate of major vascular events ($P = .002$), with no increase in bleeding. In patients who are warfarin-adverse, aspirin after a first event of VTE therefore appears to provide protection against recurrent VTE and other major vascular events.