59. Journal Club

Mittwoch, 14.06..2023 um 19.30 Uhr online

Aspirin or Low-Molecular-Weight Heparin for Thromboprophylaxis after a Fracture

Background: Clinical guidelines recommend low-molecular-weight heparin for thromboprophylaxis in patients with fractures, but trials of its effectiveness as compared with aspirin are lacking.
Methods: In this pragmatic, multicenter, randomized, noninferiority trial, we enrolled patients 18 years of age or older who had a fracture of an extremity (anywhere from hip to midfoot or shoulder to wrist) that had been treated operatively or who had any pelvic or acetabular fracture. Patients were randomly assigned to receive low-molecular-weight heparin (enoxaparin) at a dose of 30 mg twice daily or aspirin at a dose of 81 mg twice daily while they were in the hospital. After hospital discharge, the patients continued to receive thromboprophylaxis according to the clinical protocols of each hospital. The primary outcome was death from any cause at 90 days. Secondary outcomes were nonfatal pulmonary embolism, deep-vein thrombosis, and bleeding complications.
Results: A total of 12,211 patients were randomly assigned to receive aspirin (6101 patients) or low-molecular-weight heparin (6110 patients). Patients had a mean (±SD) age of 44.6±17.8 years, 0.7% had a history of venous thromboembolism, and 2.5% had a history of cancer. Patients received a mean of 8.8±10.6 in-hospital thromboprophylaxis doses and were prescribed a median 21-day supply of thromboprophylaxis at discharge. Death occurred in 47 patients (0.78%) in the aspirin group and in 45 patients (0.73%) in the low-molecular-weight-heparin group (difference, 0.05 percentage points; 96.2% confidence interval, -0.27 to 0.38; P<0.001 for a noninferiority margin of 0.75 percentage points). Deep-vein thrombosis occurred in 2.51% of patients in the aspirin group and 1.71% in the low-molecular-weight-heparin group (difference, 0.80 percentage points; 95% CI, 0.28 to 1.31). The incidence of pulmonary embolism (1.49% in each group), bleeding complications, and other serious adverse events were similar in the two groups.
Conclusions: In patients with extremity fractures that had been treated operatively or with any pelvic or acetabular fracture, thromboprophylaxis with aspirin was noninferior to low-molecular-weight heparin in preventing death and was associated with low incidences of deep-vein thrombosis and pulmonary embolism and low 90-day mortality.

Fazit:

Wir würden uns nicht trauen, ASS im (noch) „Off-Label-Use“ gegen ein von der Klinik empfohlenes NMH auszutauschen.
Im Endeffekt ist es eine gemeinsame Entscheidung mit dem Patienten, wie lange was genommen wird.

Evaluating the Association Between Low-Density Lipoprotein Cholesterol Reduction and Relative and Absolute Effects of Statin Treatment

Abstract

Importance The association between statin-induced reduction in low-density lipoprotein cholesterol (LDL-C) levels and the absolute risk reduction of individual, rather than composite, outcomes, such as all-cause mortality, myocardial infarction, or stroke, is unclear.

Objective To assess the association between absolute reductions in LDL-C levels with treatment with statin therapy and all-cause mortality, myocardial infarction, and stroke to facilitate shared decision-making between clinicians and patients and inform clinical guidelines and policy.

Data Sources PubMed and Embase were searched to identify eligible trials from January 1987 to June 2021.

Study Selection Large randomized clinical trials that examined the effectiveness of statins in reducing total mortality and cardiovascular outcomes with a planned duration of 2 or more years and that reported absolute changes in LDL-C levels. Interventions were treatment with statins (3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitors) vs placebo or usual care. Participants were men and women older than 18 years.

Data Extraction and Synthesis Three independent reviewers extracted data and/or assessed the methodological quality and certainty of the evidence using the risk of bias 2 tool and Grading of Recommendations, Assessment, Development and Evaluation. Any differences in opinion were resolved by consensus. Meta-analyses and a meta-regression were undertaken.

Main Outcomes and Measures Primary outcome: all-cause mortality. Secondary outcomes: myocardial infarction, stroke.

Findings Twenty-one trials were included in the analysis. Meta-analyses showed reductions in the absolute risk of 0.8% (95% CI, 0.4%-1.2%) for all-cause mortality, 1.3% (95% CI, 0.9%-1.7%) for myocardial infarction, and 0.4%(95% CI, 0.2%-0.6%) for stroke in those randomized to treatment with statins, with associated relative risk reductions of 9% (95% CI, 5%-14%), 29% (95% CI, 22%-34%), and 14% (95% CI, 5%-22%) respectively. A meta-regression exploring the potential mediating association of the magnitude of statin-induced LDL-C reduction with outcomes was inconclusive.

Conclusions and Relevance The results of this meta-analysis suggest that the absolute risk reductions of treatment with statins in terms of all-cause mortality, myocardial infarction, and stroke are modest compared with the relative risk reductions, and the presence of significant heterogeneity reduces the certainty of the evidence. A conclusive association between absolute reductions in LDL-C levels and individual clinical outcomes was not established, and these findings underscore the importance of discussing absolute risk reductions when making informed clinical decisions with individual patients.

Fazit:

Das Cholesterin ist den meisten Patienten wichtig. Von Industrieseite ist auch eine eindeutige Interessenlage da, Cholesterin so intensive wie möglich zu senken. In der Primärprävention ist es nicht effektiv, in der Sekundärprävention nur relativ und abhängig von Co-Faktoren.
Insgesamt setzen wir Cholesterinsenker möglichst oft und sehr gerne ab.

Efficacy and safety of lasmiditan in patients using concomitant migraine preventive medications: findings from SAMURAI and SPARTAN, two randomized phase 3 trials

Abstract

Objective: To study the efficacy and safety of lasmiditan for acute treatment of migraine in patients using migraine preventive medications.

Background: While lasmiditan has been proven to be an effective acute treatment for migraine, its effectiveness has not been examined when used concurrently with migraine preventives.

Methods: SAMURAI and SPARTAN were similarly designed, double-blind, phase 3, placebo-controlled studies of patients 18 years or older with 3 to 8 migraine attacks per month. Patients were randomized to treat a migraine attack with oral lasmiditan 50 mg (SPARTAN only), 100 mg, 200 mg, or placebo. Migraine preventives were allowed as long as doses were stable for 3 months prior to screening and were unchanged during the study. Preventive medications with established or probable efficacy, as recommended by the American Academy of Neurology, the American Headache Society, and the European Headache Federation, plus botulinum toxin type A and candesartan, were included. Within the subgroups of patients using and not using preventive therapies, lasmiditan and placebo groups were analyzed for the outcome of pain-free at 2 h and other efficacy outcomes. The subgroups of patients using and not using preventive therapies were compared and interaction p-values were calculated for safety and efficacy outcomes.

Results: In these trials, 698 of 3981 patients (17.5%) used migraine preventive treatments. Among patients using preventives, all lasmiditan doses resulted in significantly more patients being pain-free at 2 h, compared to placebo ($p < 0.05$). Primary efficacy outcome (pain-free at 2 h), key secondary outcome (most bothersome symptom-free at 2 h) and all other efficacy outcomes were not significantly different between patients using or not using migraine preventives (all interaction p-values ≥0.1). Rates of adverse events were similar for patients using and not using preventive medications.

Conclusions: Lasmiditan was more effective than placebo for the acute treatment of migraine in patients concurrently using migraine preventive medications. Lasmiditan efficacy and safety measures were similar for patients using and not using preventive medications.

Trial registration: SAMURAI (NCT02439320) and SPARTAN (NCT02605174). Registered 18 March 2015. Keywords: Acute treatment, Concomitant, Ditan, Efficacy, Lasmiditan, Migraine, Migraine medication, Migraine

Fazit:

Im Prinzip sollten erst alle Triptane versucht werden, dann kann man Lasmiditan probieren. Die Wirkung (NNT 8) ist recht überschaubar. Besser als Triptane sind sie offensichtlich nicht.

Albuminuria-lowering effect of dapagliflozin, exenatide, and their combination in patients with type 2 diabetes: A randomized cross-over clinical study

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Ziel
Bewertung der Albuminurie-senkenden Wirkung von Dapagliflozin, Exenatid und der Kombination von Dapagliflozin und Exenatid bei Patienten mit Typ-2-Diabetes und Mikroalbuminurie oder Makroalbuminurie.

Methoden
Teilnehmer mit Typ-2-Diabetes, einer geschätzten glomerulären Filtrationsrate (eGFR) von mehr als 30 ml/min/1,73 m2 und einem Albumin-Kreatinin-Verhältnis (UACR) im Urin von 3,5 mg/mmol bis 100 mg/mmol absolvierten drei 6-wöchige Behandlungen, in denen Dapagliflozin 10 mg/Tag, Exenatid 2 mg/Woche und beide Arzneimittel kombiniert verabreicht wurden. (Wash-out zwischen Therapien: 9 Wochen) Der primäre Endpunkt war die prozentuale Änderung der UACR. Zu den sekundären Endpunkten gehörten Blutdruck, HbA1c, Körpergewicht, extrazelluläres Volumen, fraktionierte Lithiumausscheidung und renale hämodynamische Variablen, bestimmt durch Magnetresonanztomographie.

Ergebnisse
20 Patienten wurden aufgenommen, die insgesamt 53 Behandlungen abgeschlossen haben. Die mittlere prozentuale Veränderung der UACR gegenüber dem Ausgangswert betrug –21,9 % (95 %-KI: –34,8 % bis –6,4 %) unter Dapagliflozin im Vergleich zu –7,7 % (95 %-KI: –23,5 % bis 11,2 %) unter Exenatid und –26,0 % (95). % KI: –38,4 % bis –11,0 %) während der Behandlung mit Dapagliflozin-Exenatid. Im Vergleich zu Dapagliflozin oder Exenatid allein wurde unter der Behandlung mit Dapagliflozin kombiniert mit Exenatid stärkere Senkung des systolischen Blutdrucks, des Körpergewichts und der eGFR beobachtet. Der renale Blutfluss und der effektive renale Plasmafluss (ERPF) veränderten sich bei beiden Behandlungsschemata nicht signifikant. Allerdings zeigten alle bis auf vier bzw. zwei Patienten in der Dapagliflozin- bzw. Dapagliflozin-Exenatid-Gruppe eine Verringerung des ERPF. Die Filtrationsfraktion veränderte sich während der Behandlung mit Dapagliflozin oder Exenatid nicht und nahm während der Behandlung mit Dapagliflozin und Exenatid ab (–1,6 % [95 %-KI: –3,2 % bis –0,01 %]; P = 0,048).

Schlussfolgerungen
Bei Teilnehmern mit Typ-2-Diabetes und Albuminurie verringerte die Behandlung mit Dapagliflozin, Exenatid und Dapagliflozin-Exenatid die Albuminurie, wobei die Verringerung in der kombinierten Dapagliflozin-Exenatid-Gruppe am größten war.

Fazit:

Die sehr kleine Studie ist mit Vorsicht zu betrachten. Der Einsatz bei Nierenerkrankungen scheint noch sehr gehypt zu werden. Wir sind sehr zurückhaltend.

The Colorectal cancer RISk Prediction (CRISP) trial: a randomised controlled trial of a decision support tool for risk-stratified colorectal cancer screening

BACKGROUND: A risk-stratified approach to colorectal cancer (CRC) screening could result in a more acceptable balance of benefits and harms, and be more cost-effective.
AIM: To determine the effect of a consultation in general practice using a computerised risk assessment and decision support tool (Colorectal cancer RISk Prediction, CRISP) on risk-appropriate CRC screening.
DESIGN AND SETTING: Randomised controlled trial in 10 general practices in Melbourne, Australia, from May 2017 to May 2018.
METHOD: Participants were recruited from a consecutive sample of patients aged 50-74 years attending their GP. Intervention consultations included CRC risk assessment using the CRISP tool and discussion of CRC screening recommendations. Control
group consultations focused on lifestyle CRC risk factors. The primary outcome was risk-appropriate CRC screening at 12 months.
RESULTS: A total of 734 participants (65.1% of eligible patients) were randomised (369 intervention, 365 control); the primary
outcome was determined for 722 (362 intervention, 360 control). There was a 6.5% absolute increase (95% confidence interval [CI] =
-0.28 to 13.2) in risk-appropriate screening in the intervention compared with the control group (71.5% versus 65.0%; odds ratio [OR]
1.36, 95% CI = 0.99 to 1.86, P = 0.057). In those due CRC screening during follow-up, there was a 20.3% (95% CI = 10.3 to 30.4)
increase (intervention 59.8% versus control 38.9%; OR 2.31, 95% CI = 1.51 to 3.53, P<0.001) principally by increasing faecal occult
blood testing in those at average risk.
CONCLUSION: A risk assessment and decision support tool increases risk-appropriate CRC screening in those due screening. The
CRISP intervention could commence in people in their fifth decade to ensure people start CRC screening at the optimal age with the
most cost-effective test.

Fazit:

Der Wirkungsgrad der Früherkennungsuntersuchung ist überschaubar. Das scheint sich durch den Rechner zu bestätigen. Möglicherweise ein Tool, um PatientInnen in ihrer individuellen Entscheidung zu unterstützen. Es ersetzt aber nicht unsere persönliche Beratung des einzelnen Patienten.
Im Rechner wird der ifobt-Stuhltest im Endeffekt priorisiert.