

Hot Articles

“September|2017”

Health Science



Title: [Oxygen uptake at aerobic threshold is inversely associated with fatal cardiovascular and all-cause mortality events](#)

Author: Setor K. Kunutsor , Sudhir Kurl, Hassan Khan, Francesco Zaccardi, Rainer Rauramaa & Jari A. Laukkanen

Journal: Annals of Medicine

Volume: Published online: 22 Aug 2017

Doi: 10.1080/07853890.2017.1367958

Abstract

Purpose: We aimed to assess the associations of oxygen uptake at aerobic threshold (VO₂ at AT) with cardiovascular and all-cause mortality.

Design: VO₂ at AT was assessed in 1663 middle-aged men in a cohort study. Hazard ratios (HRs) were calculated for sudden cardiac death (SCD), fatal coronary heart disease (CHD) and cardiovascular disease (CVD) and all-cause mortality.

Results: During a median follow-up of 25.6 years, 138 SCDs, 209 fatal CHDs, 333 fatal CVDs and 719 all-cause mortality events occurred. On adjustment for established risk factors, the HRs (95% CIs) for SCD, fatal CHD, fatal CVD and all-cause mortality were 0.48 (0.28–0.82), 0.48 (0.31–0.74), 0.57 (0.41–0.79) and 0.66 (0.53–0.82), respectively comparing extreme quartiles of VO₂ at AT. On further adjustment for peak VO₂, the HRs were 0.87 (0.48–1.56), 0.83 (0.52–1.34), 0.91 (0.63–1.30) and 0.88 (0.69–1.12), respectively. Addition of VO₂ at AT to a standard CVD mortality risk prediction model was associated with a C-index change of 0.0085 (95% CI: –0.0002–0.0172; p = .05) at 25 years.

Conclusions: VO₂ at AT is inversely associated with cardiovascular and all-cause mortality events, but the associations are partly dependent on peak VO₂. VO₂ at AT may improve the prediction of the long-term risk for CVD mortality.

Database

Taylor & Francis Online Journals

Title: [Selective induction of apoptosis in MCF7 cancer-cell by targeted liposomes functionalised with mannose-6-phosphate](#)

Author: Cristina Minnelli, Laura Cianfruglia, Emiliano Laudadio, Roberta Galeazzi, Michela Pisani, Emanuela Crucianelli, Davide Bizzaro, Tatiana Armeni & Giovanna Mobbili

Journal: Journal of Drug Targeting

Volume: Published online: 25 Aug 2017

Doi: 10.1080/1061186X.2017.1365873

Abstract

Liposomes are versatile platforms to carry anticancer drugs in targeted drug delivery; they can be surface modified by different strategies and, when coupled with targeting ligands, are able to increase cellular internalisation and organelle-specific drug delivery. An interesting strategy of antitumoral therapy could involve the use of lysosomotropic ligand-targeted liposomes loaded with molecules, which can induce lysosomal membrane permeabilization (LMP), leakage of cathepsins into the cytoplasm and subsequent apoptosis. We have previously demonstrated the ability of liposomes functionalised with a mannose-6-phosphate to reach lysosomes; in this research we compare the behaviour of M6P-modified and non-functionalised liposomes in MCF7 tumour cell and in HDF normal cells. With this aim, we first demonstrated by Western blotting the overexpression of mannose-6-phosphate/insulin-like growth factor (M6P/IGF-II) receptor in MCF7. Then, we prepared calcein-loaded liposomes and we revealed the increased uptake of M6P-functionalised liposomes in MCF7 cells respect to HDF cells by flow cytometry analysis. Finally, we loaded functionalised and not functionalised liposomes with N-hexanoyl-d-erythro-sphingosine (C6Cer), able to initiate LMP-induced apoptosis; after having studied the stability of both vesicles in the presence of serum by Dynamic Light Scattering and Spectrophotometric turbidity measurements, we showed that ceramide-loaded M6P-liposomes significantly increased apoptosis in MCF7 with respect to HDF cells.

Database

Taylor & Francis Online Journals

Title: [Stress hormones at rest and following exercise testing predict coronary artery disease severity and outcome](#)

Author: Dejana Popovic , Svetozar Damjanovic, Tea Djordjevic, Dejana Martic, Svetlana Ignjatovic, Neda Milinkovic, Marko Banovic, Ratko Lasica, Milan Petrovic, Marco Guazzi & Ross Arena

Journal: Stress

Volume: Published online: 28 Aug 2017

Doi: 10.1080/10253890.2017.1368488

Abstract

Objectives: Despite considerable knowledge regarding the importance of stress in coronary artery disease (CAD) pathogenesis, its underestimation persists in routine clinical practice, in part attributable to lack of a standardized, objective assessment. The current study examined the ability of stress hormones to predict CAD severity and prognosis at basal conditions as well as during and following an exertional stimulus.

Materials and methods: Forty Caucasian subjects with significant coronary artery lesions ($\geq 50\%$) were included. Within 2 months of coronary angiography, cardiopulmonary exercise testing (CPET) on a recumbent ergometer was performed in conjunction with stress echocardiography (SE). At rest, peak and after 3 min of recovery following CPET, plasma levels of cortisol, adrenocorticotrophic hormone (ACTH) and NT-pro-brain natriuretic peptide (NT-pro-BNP) were measured by immunoassay sandwich technique, radioimmunoassay, and radioimmunometric technique, respectively. Subjects were subsequently followed a mean of 32 ± 10 months.

Results and discussion: Mean ejection fraction was $56.7 \pm 9.6\%$. Subjects with 1–2 stenotic coronary arteries (SCA) demonstrated a significantly lower plasma cortisol levels during CPET compared to those with 3-SCA ($p < .05$), whereas ACTH and NT-pro-BNP were not significantly different ($p > .05$). Among CPET, SE, and hormonal parameters, cortisol at rest and during CPET recovery demonstrated the best predictive value in distinguishing between 1-, 2-, and 3-SCA [area under ROC curve 0.75 and 0.77 (SE = 0.11, 0.10; $p = .043, .04$) for rest and recovery, respectively]. Δ Cortisol peak/rest predicted cumulative cardiac events (area under ROC curve 0.75, SE = 0.10, $p = .049$).

Conclusions: Cortisol at rest and following an exercise test holds predictive value for CAD severity and prognosis, further demonstrating a link between stress and unwanted cardiac events.

Database

Taylor & Francis Online Journals

Title: [Second-line treatments of small-cell lung cancers](#)

Author: Nathalie Baize, Isabelle Monnet, Laurent Greillier, Gilles Quere, Mallorie Kerjouan, Henri Janicot, Alain Vergnenegre, Jean Bernard Auliac & Christos Chouaid

Journal: Expert Review of Anticancer Therapy

Volume: Accepted author version posted online: 29 Aug 2017

Doi: 10.1080/14737140.2017.1372198

Abstract

Introduction: Second-line therapies for relapsed small cell lung cancer (SCLC) patients remain a challenge, with limited clinical benefit because of rapid tumor growth, early dissemination and the development of drug resistance during the disease. Recent developments in genomic sequencing have provided further insight into the biology of the disease, identifying new targets and new pathways.

Areas covered: This review details chemotherapy, targeted therapies and immune-checkpoint blockades that have been investigated as second-line treatments for SCLC patients using a PubMed search (period 1990 – 2016, terms used: SCLC, treatments, second line, therapy).

Expert commentary: Recent genomic, proteomic and preclinical studies have identified novel therapeutic strategies currently being evaluated in clinical trials. Promising approaches for SCLC management include delta-like ligand-3 (DLL3)-targeted antibody–drug conjugate, combination targeted therapies, or targeted therapy–chemotherapy with an additive effect superior to the efficacy of single agents. The blockade of immune checkpoints has yielded promising preliminary results and is being investigated in ongoing trials. The inclusion of SCLC patients relapsing after platin-doublet induction in well-designed clinical trials remains a major challenge.

Database

Taylor & Francis Online Journals

Title: [Smoking Cessation Among Methadone-Maintained Patients: A Meta-Analysis](#)

Author: Anne Yee, Moey Chee Hoong, Yong Chen Joyce & Huai Seng Loh FRACGP

Journal: Substance Use & Misuse

Volume: Published online: 31 Aug 2017

Doi: 10.1080/10826084.2017.1342661

Abstract

Background: Nicotine use disorder is highly prevalent among methadone maintenance patients with its tobacco-related problems. However, the treatment modalities for nicotine use disorder remain limited.

Objective: Our meta-analysis aims to examine the effectiveness of smoking cessation treatment in this group of patients.

Methods: A total of 1358 participants were recruited from 9 eligible studies, published from the start of studies in this field till Feb 2016, identified from PubMed, OVID, EMBASE and Google Scholar databases. Two independent reviewers assessed the eligibility of each report based on predefined inclusion criteria. Pooled odd ratios or weighted mean difference was performed using random effects.

Results: The treatments for smoking cessation among MMT patients are behavioral and pharmacological therapies. Smoking cessation was better achieved with nicotine replacement therapy (NRT) especially with adjunctive behavioral therapy. The pooled odds ratio of smokers' abstinence of smoking by the end of the treatment between NRT and placebo group was 6.32 (95% CI = 1.18 to 33.75, $p = 0.03$) and is statistically significant. Any additional behavior therapy among MMT patients who received the smoking cessation pharmacotherapy as the primary treatment was not better than those who only received standard care (Odds ratio was 2.53, 95% CI = 0.75 to 8.56, $p = 0.14$).

Conclusions: Although NRT is proven to be effective in smoking cessation, more studies are warranted to prove the effects of other pharmacotherapy in smoking cessation.

Database

Taylor & Francis Online Journals

Title: [Lysosomal targeting strategies for design and delivery of bioactive for therapeutic interventions](#)

Author: Ankur Sharma, Kalpesh Vaghasiya, Eupa Ray & Rahul Kumar Verma

Journal: Journal of Drug Targeting

Volume: Accepted author version posted online: 01 Sep 2017

Doi: 10.1080/1061186X.2017.1374390

Abstract

Lysosomes are of particular interest for the design and delivery of pH dependent pro-drugs, enhancing selectivity and developing strategies to inhibit drug degradation inside the cells. There is great potential to bring intracellular drug delivery and distribution using nano-therapeutic approaches to target lysosomes for therapeutic interventions. Lysosomal targeting strategies involve two contrasting facets. One aspect is to directly target therapeutics to the lysosome through receptor-mediated endocytosis and the other facet involves strategies, which ensure escape from the lysosome in order to prevent their degradation, so that therapeutics may remain intact and available in the cytosol for their further action. It provides a unique opportunity to explore novel treatment strategies and design future drugs for effective treatment of lysosome related diseases especially lysosomal storage disorders (LSD), cancer, inflammatory, neurodegenerative conditions (Parkinson's, Alzheimer's, and Huntington's diseases) and auto-immune diseases. In this review, we illustrate the fundamentals of membrane trafficking, subcellular organization, strategies to target lysosomes and its implications for the advance design of efficient drug delivery vectors for safe and effective therapies.

Database

Taylor & Francis Online Journals

Title: [Screening for Transplant Renal Artery Stenosis: Ultrasound-Based Stenosis Probability Stratification](#)
Author: Ghaneh Fananapazir, et al.
Journal: American Journal of Roentgenology
Volume: Aug 31, 2017 (Ahead of Print)
Doi: 1-10. 10.2214/AJR.17.17913

Abstract

OBJECTIVE. The objective of our study was to evaluate which spectral Doppler ultrasound parameters are useful in patients with clinical concern for transplant renal artery stenosis (TRAS) and create mathematically derived prediction models that are based on these parameters.

MATERIALS AND METHODS. The study subjects included 120 patients with clinical signs of renal dysfunction who had undergone ultrasound followed by angiography (either digital subtraction angiography or MR angiography) between January 2005 and December 2015. Five ultrasound variables were evaluated: ratio of highest renal artery velocity to iliac artery velocity, highest renal artery velocity, spectral broadening, resistive indexes, and acceleration time. Angiographic studies were categorized as either showing no stenosis or showing stenosis. Reviewers assessed the ultrasound examinations for TRAS using all five variables, which we refer to as the full model, and using a reduced number of variables, which we refer to as the reduced-variable model; sensitivities and specificities were generated.

RESULTS. Ninety-seven patients had stenosis and 23 had no stenosis. The full model had a sensitivity and specificity of 97% and 91%, respectively. The reduced-variable model excluded the ratio and resistive index variables without affecting sensitivity and specificity. We applied cutoff values to the variables in the reduced-variable model, which we refer to as the simple model. Using these cutoff values, the simple model showed a sensitivity and specificity of 96% and 83%. The simple model was able to categorize patients into four risk categories for TRAS: low, intermediate, high, and very high risk.

CONCLUSION. We propose a simple model that is based on highest renal artery velocity, distal spectral broadening, and acceleration time to classify patients into risk categories for TRAS.

Database

American Roentgen Ray Society

Title: [Can rapid negative exclusion of blood cultures by a molecular method, enzyme template generation and amplification technique \(Cognitor® Minus\), aid antimicrobial stewardship?](#)

Author: Matthew Dryden, Agnes Sitjar, Zoe Gunning, Sophie Lewis, Richard Healey, Praneeth Satchithanathan, Natalie Parker, Taryn Keyser, Kordo Saeed and Helen V. Bennett

Journal: International Journal of Pharmacy Practice

Volume: Version of Record online: 18 AUG 2017

Doi: 10.1111/ijpp.12393

Abstract

Objectives

Antimicrobial review is an important part of antimicrobial stewardship. A novel enzyme template generation and amplification technique (ETGA), the Cognitor® Minus (Momentum Bioscience, Long Hanborough, UK) test, has a 99.5% negative predictive value for bacteraemia and fungaemia. This observational study asked two questions: (1) Does a negative ETGA, indicating no bacteraemia or fungaemia, aid antimicrobial review within 48 h of admission; (2) In this real-life clinical setting, does a negative ETGA mean no bacteraemia or fungaemia?

Methods

Consecutive blood cultures in patients with clinical infection were tested by ETGA. Negative results indicating an absence of bacteraemia or fungaemia were reviewed by the clinical infection team. Antibiotics were reviewed in these patients, and the role of the ETGA result in antibiotic change was recorded. Patients were followed up for a week.

Key findings

A total of 197 of 246 samples gave a negative result by ETGA. This led to a positive stewardship outcome (antimicrobials changed) in 145 (73.6%) and negative stewardship outcome (empirical antimicrobials continued) in 47 (23.9%). Of the positive stewardship outcomes, the ETGA result supported the decision not to start antimicrobials in 21 (10.7%) patients, to stop antimicrobials in 21 (10.7%), to switch from IV to oral antimicrobials in 103 (52.2%) or to discharge or leave the patient at home in 58 cases (29.4%).

Conclusions

Enzyme template generation and amplification supports antimicrobial stewardship decisions and may have cost advantages in reducing unnecessary empirical antibiotics and antifungal agents and in discharging patients from hospital earlier. ETGA result was consistent with blood culture findings and gave an earlier negative result.

Database

Wiley Online Library

Title: [Perceptions of Yemeni physicians about interactions with medical representatives](#)
Author: Mahmoud A. Al-Areefi, Mohamed Izham M. Ibrahim, Mohamed Azmi A. Hassali and Abubakr A. Alfadl
Journal: Journal of Pharmaceutical Health Services Research
Volume: Version of Record online: 29 AUG 2017
Doi: 10.1111/jphs.12195

Abstract

Objective

Interaction between physicians and medical representatives (MR) is an area of controversy, which discussed heavily in the literature. However, the perspectives of physicians on the extent and composition of pharmaceutical promotion techniques have been neglected especially in developing countries. Therefore, this study aims to bridge this gap through investigating physicians' perceptions, beliefs and attitudes towards interactions with medical representatives with special emphasis on their perception about the appropriateness of accepting drug company promotions and their either positive or negative attitudes towards drug promotion activities.

Methods

This is a descriptive cross-sectional study that investigates physicians' perceptions about interactions with medical representatives. Data were collected through an anonymous survey questionnaire circulated to 610 physicians.

Key findings

Majority (85.3%) of participated physicians has positive attitudes towards interactions with medical representatives, and they disagree with the idea of banning medical representatives' visits. Also perception of the majority (60.8%) of physicians is that most promotional techniques do not pose ethical problem, and it is appropriate to accept most promotional items.

Conclusion

Majority of the physicians have positive attitudes towards interactions with MRs. Most of the physicians believe that most promotional techniques do not pose ethical problem, and it is acceptable to accept promotional items.

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Title: [Effect of Vitamin D in the Prevention of Myocardial Injury Following Elective Percutaneous Coronary Intervention: A Pilot Randomized Clinical Trial](#)

Author: Naser Aslanabadi, Iraj Jafaripor, Selda Sadeghi, Hadi Hamishehkar, Samad Ghaffari, Mehdi Toluey, Hanieh Azizi, Taher Entezari-Maleki

Journal: The Journal of Clinical Pharmacology

Volume: First Published: 25 August 2017

Doi: 10.1002/jcph.989

Abstract

Myocardial injury following elective percutaneous coronary intervention (PCI) occurs in about one-third of patients and is associated with mortality. Platelet aggregation, thrombosis formation, and inflammation are the main causes of cardiac injury during PCI. Vitamin D plays a key role in the cardiovascular system by exerting antiplatelet, anticoagulant, and anti-inflammatory properties. There is no published study that investigated the effect of vitamin D in the prevention of cardiac injury following elective PCI. In a randomized clinical trial, 99 patients admitted for elective PCI were randomized into vitamin D (n = 52) and control (n = 47) groups. The intervention group received 300 000 IU vitamin D orally 12 hours before PCI. The cardiac biomarkers were checked at baseline, 8 and 24 hours after PCI. hs-CRP was also measured at baseline and after 24 hours. The increase in CK-MB was documented in 20 patients (42%) in the control group and 18 patients (34.6%) in the intervention group (P = .417). Furthermore, the increase in cTnI occurred in 4 patients (8%) and 2 patients (3.3%) in the control and intervention groups, respectively (P = .419). No significant changes were noted in the level of cardiac biomarkers. In the vitamin D group, the mean difference in CK-MB between 8 and 24 hours was significantly lower (P = .048). The mean difference in hs-CRP was significantly lower in the vitamin D group (P = .045). This study could not show a clear effect of vitamin D in the prevention of cardiac injury during elective PCI. Further outcome-based studies are needed to describe the role of vitamin D in the prevention of periprocedural myocardial injury.

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