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## Toho Journal of Medicine Vol. 5 No. 3 掲載論文の紹介

Is Noninvasive Continuous Cardiac Output Technique Based on Pulse Wave Transit Time Applicable in Cardiac Output Monitoring during Thoracic Aortic Aneurysm Surgery?

Kajitani M, Ochiai R

Toho J Med 5 (3): 85—92, 2019

### 要約 :

**Introduction:** The present study compared the precision of estimated continuous cardiac output (esCCO) and the use of a pulmonary artery catheter (PAC) in continuous measurement of cardiac output (paCCO) in total arch replacement (TAR).

**Methods:** Cardiac output was measured continuously, using esCCO and paCCO, for 24 h from the time of arrival in the operating room until admission to the intensive care unit (ICU). Continuous cardiac output measurements obtained using the above devices were compared using Bland-Altman analysis to evaluate bias, precision, and percent error (%error) and four-quadrant plots to evaluate the concordance rate.

**Results:** The examination of 17 patients was held at 3 setting points: starting anesthesia to before cardio-pulmonary bypass (pre-CPB), after CPB to the end of surgery (post-CPB), and after ICU admission (ICU). Data were obtained at 2,513, 2,426, and 23,533 points, respectively. Bias  $\pm$  precision of esCCO to paCCO was  $-0.24 \pm 0.88$  L/min,  $0.22 \pm 1.42$  L/min,  $0.61 \pm 0.84$  L/min and % error was 48%, 56%, and 44% respectively. The concordance rate of four-quadrant plot was 64.9%, 68.0%, 73.8% respectively.

**Conclusions:** When we have compared compatibility, concordance, and trending ability of esCCO to paCCO in pre-CPB, post-CPB, and ICU, it is difficult to estimate cardiac output with esCCO during TAR. The results might have been influenced by direct effects on the cardiac contraction associated with surgical procedures, and changes in the physical properties of vascular elasticity with vascular prosthesis implantation.

**KEYWORDS:** esCCO, cardiac output, pulmonary artery catheter, total arch replacement surgery

Diagnostic and Prognostic Impacts of Six Autoantibodies against Multiple Tumor-Associated Antigens with Hepatocellular Carcinoma

Okada R, Hoshino I, Nabeya Y, Yokoi S, Kuwajima A, Tagawa M, Matsushita K, Otsuka Y, Shimada H

Toho J Med 5 (3): 93—100, 2019

### 要約 :

**Introduction:** Despite improvements in surgical techniques and other treatment modalities, the prognosis of hepatocellular carcinoma (HCC) remains poor because of late diagnosis. Recently, multiple molecular biomarkers were reported to be potential diagnostic tools for HCC.

**Methods:** We analyzed serum samples from 152 healthy controls and 94 HCC patients at the Chiba Cancer Center using an enzyme-linked immunosorbent assay. Recombinant proteins were expressed in *Escherichia coli* (*E. coli*), purified, and then used for enzyme-linked immunosorbent assay (ELISA) kit construction. For the expression and purification of recombinant proteins, the full-length cDNA of tumor-associated antigens (TAAs), including heat shock protein 70 (Hsp70), Galectin-1 (Gal-1), KM-HN-1, HCC-22-5, RalA, and NY-ESO-1, was amplified using polymerase chain reaction.

**Results:** Among HCC patients, the highest sensitivity of autoantibodies against TAAs was observed in 22 patients (23%) for Hsp70. The combination assay increased the sensitivity for all six autoantibodies to 56% (53/94). The specificity of all autoantibodies was  $>95\%$  in both cohorts. Results using cutoff values for individual autoantibodies from the validation cohort yielded similar results in the test cohort. The sensitivity of the six-autoantibody panel combined with  $\alpha$ -fetoprotein (AFP) and/or protein induced by absence of vitamin K or by antagonist-II (PIVKA-II) was significantly

higher than sensitivity achieved with AFP and/or PIVKA-II only ( $P = 0.005$ ). There were no statistically significant differences in the 3-year overall survival between the autoantibody-positive and autoantibody-negative groups.

**Conclusions:** This study showed that a panel of six autoantibodies against Hsp70, Gal-1, KM-HN-1, HCC-22-5, RaIA, and NY-ESO-1 increased the sensitivity of conventional tumor markers used to detect HCC.

**KEYWORDS:** autoantibody, biomarker, diagnosis, hepatocellular carcinoma, prognosis

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Alpha-Tocopherol Ameliorates Experimental Autoimmune Neuritis by Exerting Antioxidant Effects and Suppressing Cytokine Production

Kihara H, Konno S, Fujioka T

Toho J Med 5 (3): 101—110, 2019

要約 :

**Introduction:** Guillain-Barré syndrome (GBS) is an autoimmune neuropathy mediated by insult of antiganglioside antibodies and subsequent complement activation. Oxidative toxicity, resulting from insufficiently maintained cellular redox levels, has also been contributed to GBS pathogenesis; however, antioxidant therapy for GBS patients has not yet been established. The effectiveness of  $\alpha$ -tocopherol ( $\alpha$ T), a natural antioxidant, was evaluated as a treatment for experimental autoimmune neuritis (EAN), using an animal model of human GBS.

**Methods:** Female Lewis rats, immunized with 125  $\mu$ g of synthetic peptide from bovine P2 protein, were injected with 100 mg/kg of intraperitoneal  $\alpha$ T on only day 6 or on both days 6 and 13 post-immunization (p.i.). Lipid peroxidation products, histological alterations, and cytokine expression in the cauda equina and/or popliteal lymph nodes were sequentially evaluated.

**Results:** Flaccid paralysis developed from the tail tip at days 11-13 p.i. in both  $\alpha$ T-treated rats and nontreated control rats. The latter gradually progressed to flaccid paraplegia, and reached a peak of motor impairment on day 16 p.i., followed by spontaneous recovery. Double  $\alpha$ T administration, but not single administration, significantly improved the clinical course of EAN, decreased the level of the lipid peroxidic marker N epsilon-(hexanoyl) lysine, and suppressed mRNA expression of interferon-gamma and interleukin-10 in the popliteal lymph nodes and cauda equina. Histologically,  $\alpha$ T treatment showed reduced demyelination in the cauda equina compared to control rats.

**Conclusions:** Alpha-T ameliorated EAN by suppressing the production of pro-inflammatory cytokines and preventing oxidative damage. This demonstrates the potential of natural antioxidant treatment for GBS.

**KEYWORDS:** Guillain-Barré syndrome, experimental autoimmune neuritis, alpha-tocopherol, antioxidative effect, immunoregulatory effect

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Comparison of First- and Second-Generation Drug-Eluting Stents for Bifurcation Stenting Followed by the Final Kissing-Balloon Technique

Fujii T, Watanabe I, Nakanishi R, Amano H, Toda M, Ikeda T

Toho J Med 5 (3): 111—119, 2019

要約 :

**Introduction:** Percutaneous coronary intervention (PCI) for bifurcated lesions is challenging. We assessed the procedural performance and clinical outcomes of first- and second-generation drug-eluting stents (DES) in bifurcation stenting followed by the final kissing-balloon (FKB) technique.

**Methods:** We retrospectively analyzed 192 patients (222 lesions) who underwent PCI for bifurcated lesions. In all cases, lesions were stented, followed by FKB. Clinical outcomes were compared for the two generations—first generation (80 patients/88 lesions) vs. second generation (112 patients/134 lesions). The primary endpoint was target-lesion failure (TLF), defined as cardiac death, target-lesion revascularization, or target-lesion-related stent thrombosis at 2

years.

**Results:** TLF incidence was higher for first-generation DES than for second-generation DES (12.5% vs. 2.7%;  $P = 0.001$ ). A Cox proportional hazard analysis revealed that first-generation DES (hazard ratio [HR]: 6.32, 95% confidence interval [CI]: 1.72-23.1,  $P = 0.005$ ), age  $\geq 75$  years (HR: 1.55, 95% CI: 1.17-2.03,  $P = 0.001$ ), and left main trunk PCI (HR: 3.89, 95% CI: 1.30-11.5,  $P = 0.01$ ) were independent predictors of TLF after bifurcation stenting followed by FKB. Notably, age  $\geq 75$  years (HR: 1.70, 95% CI: 1.27-2.28,  $P < 0.01$ ) and left main trunk PCI (HR: 4.72, 95% CI: 1.35-16.5,  $P = 0.01$ ) were associated with an increased TLF for patients who were treated with first-generation DES. No prognostic factor of TLF was found for patients with second-generation DES.

**Conclusions:** In bifurcation stenting followed by FKB, outcomes are better for second-generation DES than for first-generation DES.

**KEYWORDS:** percutaneous coronary intervention, drug-eluting stent, bifurcation stenting, final kissing-balloon technique, target-lesion revascularization

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Prediction of Intraoperative Pressure Responsiveness by Dynamic Arterial Elastance in Patients Undergoing Major Abdominal Surgery

Kimura H, Maki Y, Toyoda D, Kotake Y

Toho J Med 5 (3): 120—127, 2019

要約 :

**Introduction:** Optimal arterial load is crucial to the simultaneous achievement of adequate oxygen delivery and perfusion pressure. Dynamic arterial elastance (Eadyn) has been proposed to represent arterial load. This study aimed to examine the ability of Eadyn to predict pressure responsiveness during major abdominal surgery.

**Methods:** In this analysis, we used hemodynamic data obtained from our observational study assessing the volume effect of various fluids during goal-directed fluid management in patients undergoing major gastrointestinal surgery. Stroke volume variation (SVV) and pulse pressure variation (PPV) were continuously monitored via the non-calibrating arterial pulse contour method, and Eadyn (PPV/SVV) was calculated offline. The presence of pressure responsiveness was assumed if the mean arterial pressure increased by more than 10% after fluid challenges, with a 15% or more increase in stroke volume. The predictive ability of Eadyn was assessed with receiver operator characteristics analysis.

**Results:** Positive pressure response was found in 34 of 50 fluid challenges in 33 patients. The area under the ROC curve of Eadyn for the prediction of pressure responsiveness was 0.80, suggesting the good diagnostic ability for Eadyn. The sensitivity and specificity were 0.82 and 0.63, respectively, with the best cutoff point at 1.20. The gray zone was calculated as Eadyn of 1.05-1.37, and 42% of measurements fell into this zone.

**Conclusions:** Eadyn showed moderate accuracy for the prediction of pressure responsiveness after the fluid challenge. However, a considerable fraction of the fluid challenges with positive fluid responsiveness fell within the gray zone.

**KEYWORDS:** goal-directed fluid management, preload, dynamic parameter, pressure responsiveness, arterial elastance

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