

SELECTED ABSTRACTS FROM PUBMED

1. Zhang Q, Shi Y, Xin Y, Zhang S, Zeng N, Liu M, et al. A multimodal international collaborative clinical research training program in China. *Med Educ Online*. 2019 Dec;24(1):1679944.

ABSTRACT

Background: There is a strong need to include training of research methods in training programs for physicians. International clinical research training programs (CRTP) that comprehensively introduce the methodology of clinical research and combined with practice should be a priority. However, few studies have reported a multimodal international CRTP that provides clinicians with an introduction to the quantitative and methodological principles of clinical research. Objective: This manuscript is intended to comprehensively describe the development process and the structure of this multimodal training program.

Methods: The CRTP was comprised of three distinct, sequential learning components: part 1 - a six-week online eLearning self-study; part 2 - a series of three weekly interactive synchronous webinars conducted between Durham, North Carolina, USA and Beijing, China; and part 3 - a five-day in-person workshop held at Beijing Friendship Hospital, Capital Medical University (BFH-CMU). Self-assessment quiz scores and participation rates were used to evaluate effectiveness of the training program. Participants' demographic characteristics, research experience, satisfaction and feedback on the program were collected using questionnaires.

Results: A total of 50 participants joined the CRTP. Forty-four participants (88%) completed the program satisfaction questionnaires. The average quiz score of the six eLearning units varied from 31% to 73%. Among the three components of the program, the online eLearning self-study was felt to be the most challenging. Thirty-nine (89%) of the surveyed respondents were satisfied with all components of the training program. Among the respondents, 43 (98%) felt the training was helpful in preparing them for future clinical research projects and expressed willingness to recommend the program to other colleagues.

Conclusions: We established a multimodal international collaborative training program. The program demonstrated acceptable participation rates and high satisfaction among Chinese clinicians. It provides a model that may be used by others developing similar international clinical research training programs for physicians.

Keywords: Clinical research; clinicians; international; multimodal; training program.

2. Magnin A, Iversen VC, Calvo G, Čečetková B, Dale O, Demlova R, et al. European survey on national training activities in clinical research. *Trials*. 2019 Oct 29;20(1):616.

ABSTRACT

Background: Investigator-initiated clinical studies (IITs) are crucial to generate reliable evidence that answers questions of day-to-day clinical practice. Many challenges make IITs a complex endeavour, for example, IITs often need to be multinational in order to recruit a sufficient number of patients. Recent studies highlighted that well-trained study personnel are a major factor to conduct such complex IITs successfully. As of today, however, no overview of the European training activities, requirements and career options for clinical study personnel exists.

Methods: To fill this knowledge gap, a survey was performed in all 11 member and observer countries of the European Clinical Research Infrastructure Network (ECRIN), using a standardised questionnaire. Three rounds of data collection were performed to maximize completeness and comparability of the received answers. The survey aimed to describe the landscape of academic training opportunities, to facilitate the exchange of expertise and experience among countries and to identify new fields of action.

Results: The survey found that training for Good Clinical Practice (GCP) and investigator training is offered in all but one country. A specific training for study nurses or study coordinators is also either provided or planned in ten out of eleven countries. A majority of countries train in monitoring and clinical pharmacovigilance and offer specific training for principal investigators but only few countries also train operators of clinical research organisations (CRO) or provide training for methodology and quality management systems (QMS). Minimal requirements for study-specific functions cover GCP in ten countries. Only three countries issued no requirements or recommendations regarding the continuous training of study personnel. Yet, only four countries developed a national strategy for training in clinical research and the career options for clinical researchers are still limited in the majority of countries.

Conclusions: There is a substantial and impressive investment in training and education of clinical research in the individual ECRIN countries. But so far, a systematic approach for (top-down) strategic and overarching considerations and cross-network exchange is missing. Exchange of available curricula and sets of core competencies between countries could be a starting point for improving the situation.

Keywords: Career options; Clinical research; Clinical study; Clinical study personnel; Clinical trial; ECRIN; GCP-training; Survey; Training; Training requirements.

3. Peerapornratana S, Manrique-Caballero CL, Gómez H, Kellum JA. Acute kidney injury from sepsis: current concepts, epidemiology, pathophysiology, prevention and treatment. *Kidney Int*. 2019 Nov;96(5):1083-1099.

ABSTRACT

Sepsis-associated acute kidney injury (S-AKI) is a frequent complication of the critically ill patient and is associated with unacceptable morbidity and mortality. Prevention of S-AKI is difficult because by the time patients seek medical attention, most have already developed acute kidney injury. Thus, early recognition is crucial to provide supportive treatment and limit further insults. Current diagnostic criteria for acute kidney injury has limited early detection; however, novel biomarkers of kidney stress and damage have been recently validated for risk prediction and early diagnosis of acute kidney injury in the setting of sepsis. Recent evidence shows that microvascular dysfunction, inflammation, and metabolic reprogramming are 3 fundamental mechanisms that may play a role in the development of S-AKI. However, more mechanistic studies are needed to better understand the convoluted pathophysiology of S-AKI and to translate these findings into potential treatment strategies and add to the promising pharmacologic approaches being developed and tested in clinical trials.

Keywords: epidemiology; inflammation; metabolic reprogramming; microvascular dysfunction; prevention; sepsis-associated acute kidney injury; sepsis-induced acute kidney injury; treatment.

4. *Anderson SG, Shoaib A, Myint PK, Cleland JG, Hardman SM, McDonagh TA, et al. Does rhythm matter in acute heart failure? An insight from the British Society for Heart Failure National Audit. Clin Res Cardiol. 2019 Nov;108(11):1276-1286.*

ABSTRACT

Background: Atrial fibrillation (AF) is the most common sustained arrhythmia in patients with acute heart failure (AHF). The presence of AF is associated with adverse prognosis in patients with chronic heart failure (CHF) but little is known about its impact in AHF.

Methods: Data were collected between April 2007 and March 2013 across 185 (> 95%) hospitals in England and Wales from patients with a primary death or a discharge diagnosis of AHF. We investigated the association between the presence of AF and all-cause mortality during the index hospital admission, at 30 days and 1 year post-discharge.

Results: Of 96,593 patients admitted with AHF, 44,642 (46%) were in sinus rhythm (SR) and 51,951 (54%) in AF. Patients with AF were older (mean age 79.8 (79.7-80) versus 74.7 (74.5-74.7) years; $p < 0.001$), than those in SR. In a multivariable analysis, AF was independently associated with mortality at all time points, in hospital (HR 1.15, 95% CI 1.09-1.21, $p < 0.0001$), 30 days (HR 1.13, 95% CI 1.08-1.19, $p < 0.0001$), and 1 year (HR 1.09, 95% CI 1.05-1.12, $p < 0.0001$). In subgroup analyses, AF was independently associated with worse 30-day outcome irrespective of sex, ventricular phenotype and in all age groups except in those aged between 55 and 74 years.

Conclusion: AF is independently associated with adverse prognosis in AHF during admission and up to 1 year post-discharge. As the clinical burden of concomitant AF and AHF increases, further refinement in the detection, treatment and prevention of AF-related complications may have a role in improving patient outcomes.

Keywords: Acute heart failure; Atrial fibrillation; Mortality; Prognosis.

5. *Vidal-Perez R, Casas CAJ, Agra-Bermejo RM, Alvarez-Alvarez B, Grapsa J, Fontes-Carvalho R, et al. Myocardial infarction with non-obstructive coronary arteries: A comprehensive review and future research directions. World J Cardiol. 2019 Dec 26;11(12):305-315.*

ABSTRACT

Acute coronary syndromes constitute a variety of myocardial injury presentations that include a subset of patients presenting with myocardial infarction with non-obstructive coronary arteries (MINOCA). This acute coronary syndrome differs from type 1 myocardial infarction (MI) regarding patient characteristics, presentation, pathophysiology, management, treatment, and prognosis. Two-thirds of MINOCA subjects present ST-segment elevation; MINOCA patients are younger, are more often female and tend to have fewer cardiovascular risk factors. Moreover, MINOCA is a working diagnosis, and defining the aetiological mechanism is relevant because it affects patient care and prognosis. In the absence of relevant coronary artery disease, myocardial ischaemia might be triggered by an acute event in epicardial coronary arteries, coronary microcirculation, or both. Epicardial causes of MINOCA include coronary plaque disruption, coronary dissection, and coronary spasm. Microvascular MINOCA mechanisms involve microvascular coronary spasm, takotsubo syndrome (TTS), myocarditis, and coronary thromboembolism. Coronary angiography with non-significant coronary stenosis and left ventriculography are first-line tests in the differential study of MINOCA patients. The diagnostic arsenal includes invasive and non-invasive techniques. Medical history and echocardiography can help indicate vasospasm or thrombosis, if one finite coronary territory is affected, or specify TTS if apical ballooning is present. Intravascular ultrasound, optical coherence tomography, and provocative testing are encouraged. Cardiac magnetic resonance is a cornerstone in myocarditis diagnosis. MINOCA is not a benign diagnosis, and its polymorphic forms differ in prognosis. MINOCA care varies across centres, and future multi-centre clinical trials with standardized criteria may have a positive impact on defining optimal cardiovascular care for MINOCA patients.

Keywords: Management; Myocardial infarction; Myocardial infarction with non-obstructive coronary arteries; Non-obstructive coronary; Prognosis.

6. *Seferović PM, Coats AJS, Ponikowski P, Filippatos G, Huelsmann M, Jhund PS, et al. European Society of*

Cardiology/Heart Failure Association position paper on the role and safety of new glucose-lowering drugs in patients with heart failure. Eur J Heart Fail. 2020 Feb;22(2):196-213.

ABSTRACT

Type 2 diabetes mellitus (T2DM) is common in patients with heart failure (HF) and associated with considerable morbidity and mortality. Significant advances have recently occurred in the treatment of T2DM, with evidence of several new glucose-lowering medications showing either neutral or beneficial cardiovascular effects. However, some of these agents have safety characteristics with strong practical implications in HF [i.e. dipeptidyl peptidase-4 (DPP-4) inhibitors, glucagon-like peptide-1 receptor agonists (GLP-1 RA), and sodium-glucose co-transporter type 2 (SGLT-2) inhibitors]. Regarding safety of DPP-4 inhibitors, saxagliptin is not recommended in HF because of a greater risk of HF hospitalisation. There is no compelling evidence of excess HF risk with the other DPP-4 inhibitors. GLP-1 RAs have an overall neutral effect on HF outcomes. However, a signal of harm suggested in two small trials of liraglutide in patients with reduced ejection fraction indicates that their role remains to be defined in established HF. SGLT-2 inhibitors (empagliflozin, canagliflozin and dapagliflozin) have shown a consistent reduction in the risk of HF hospitalisation regardless of baseline cardiovascular risk or history of HF. Accordingly, SGLT-2 inhibitors could be recommended to prevent HF hospitalisation in patients with T2DM and established cardiovascular disease or with multiple risk factors. The recently completed trial with dapagliflozin has shown a significant reduction in cardiovascular mortality and HF events in patients with HF and reduced ejection fraction, with or without T2DM. Several ongoing trials will assess whether the results observed with dapagliflozin could be extended to other SGLT-2 inhibitors in the treatment of HF, with either preserved or reduced ejection fraction, regardless of the presence of T2DM. This position paper aims to summarise relevant clinical trial evidence concerning the role and safety of new glucose-lowering therapies in patients with HF.

Keywords: Cardiovascular risk; Clinical trial; Dipeptidyl peptidase-4 inhibitor; Glucagon-like peptide-1 receptor agonist; Heart failure; Hospitalisation; Sodium-glucose co-transporter type 2 inhibitor; Type 2 diabetes mellitus.

7. *Ku S-Y, Gleave ME, Beltran H. Towards precision oncology in advanced prostate cancer. Nat Rev Urol. 2019 Nov;16(11):645-654.*

ABSTRACT

Metastatic biopsy programmes combined with advances in genomic sequencing have provided new insights into the molecular landscape of castration-resistant prostate cancer (CRPC), identifying actionable targets, and emerging resistance mechanisms. The detection of DNA repair aberrations, such as mutation of BRCA2, could help select

patients for poly(ADP-ribose) polymerase (PARP) inhibitor or platinum chemotherapy, and mismatch repair gene defects and microsatellite instability have been associated with responses to checkpoint inhibitor immunotherapy. Poor prognostic features, such as the presence of RB1 deletion, might help guide future therapeutic strategies. Our understanding of the molecular features of CRPC is now being translated into the clinic in the form of increased molecular testing for use of these agents and for clinical trial eligibility. Genomic testing offers opportunities for improving patient selection for systemic therapies and, ultimately, patient outcomes. However, challenges for precision oncology in advanced prostate cancer still remain, including the contribution of tumour heterogeneity, the timing and potential cooperation of multiple driver gene aberrations, and diverse resistant mechanisms. Defining the optimal use of molecular biomarkers in the clinic, including tissue-based and liquid biopsies, is a rapidly evolving field.

8. *Davila JR, Mruthyunjaya P. Updates in imaging in ocular oncology. F1000Res. 2019 Oct 1;8:F1000 Faculty Rev-1706.*

ABSTRACT

Innovations in ophthalmic imaging have made a profound impact on the diagnosis and treatment of ophthalmic disease. In ocular oncology, the development of optical coherence tomography with enhanced depth imaging and swept source technologies has made it possible to visualize the anatomical characteristics of retinoblastoma and uveal melanoma with a level of detail previously unobtainable on clinical exam alone. As a result, our understanding of the pathophysiology of vision loss in choroidal melanoma in particular has improved. These modalities have also helped identify fundoscopically "invisible" tumors and risk stratify pre-malignant choroidal lesions, making a strong case for their inclusion in all screening evaluations. Optical coherence tomography angiography, on the other hand, has allowed non-invasive imaging of the retinal and uveal vasculatures, providing insight into vascular changes associated with malignant transformation and vision loss following exposure to radiation. While the impact of new imaging technologies on clinical outcomes and overall survival in ocular oncology has yet to be determined, several reports cited herein offer promising results.

Keywords: Ocular oncology; angiography; melanoma; ocular surface squamous neoplasia; optical coherence tomography; radiation retinopathy; retinoblastoma.

9. *Abudu RM, Cira MK, Pyle DHM, Duncan K. Landscape of Global Oncology Research and Training at National Cancer Institute-Designated Cancer Centers: Results of the 2018 to 2019 Global Oncology Survey. J Glob Oncol. 2019 Nov;5:1-8.*

ABSTRACT

Purpose: The National Cancer Institute (NCI)-Designated Cancer Centers (NDCCs) are active in global oncology

research and training, leading collaborations to support global cancer control. To better understand global oncology activities led by NDCCs, the NCI Center for Global Health collaborated with ASCO to conduct the 2018/2019 NCI/ASCO Global Oncology Survey of NDCCs.

Methods: Seventy NDCCs received a two-part survey that focused on global oncology programs at NDCCs and non-National Institutes of Health (NIH)-funded global oncology projects with an international collaborator led by the NDCCs. Sixty-seven NDCCs responded to the survey. Data were coded and analyzed by NCI-Center for Global Health staff.

Results: Thirty-three NDCCs (47%) reported having a global oncology program, and 61 (87%) reported a collective total of 613 non-NIH-funded global oncology projects. Of the NDCCs with global oncology programs, 17 reported that trainees completed rotations outside the United States and the same number enrolled trainees from low- and middle-income countries (LMIC). Primary focus areas of non-NIH-funded projects were research (469 [76.5%]) and capacity building or training (197 [32.1%]). Projects included collaborators from 110 countries; 68 of these were LMIC.

Conclusion: This survey shows that there is a substantial amount of global oncology research and training conducted by NDCCs and that much of this is happening in LMIC. Trends in these data reflect those in recent literature: The field of global oncology is growing, advancing scientific knowledge, contributing to building research and training capacity in LMIC, and becoming a recognized career path. Results of the 2018 Global Oncology Survey can be used to foster opportunities for NDCCs to work collaboratively on activities and to share their findings with relevant stakeholders in their LMIC collaborator countries.

10. *Yalcin S, Gumus M, Oksuzoglu B, Ozdemir F, Evrensel T, Sarioglu AA, et al. Nutritional Aspect of Cancer Care in Medical Oncology Patients. Clin Ther. 2019 Nov;41(11):2382-2396.*

ABSTRACT

Purpose: Awareness of advances in the nutritional aspects of cancer care and translation of this information into

clinical practice are important for oncology practitioners to effectively couple oncologic and nutritional approaches throughout the cancer journey. The goal of this consensus statement by a panel of medical oncologists was to provide practical and implementable guidance addressing nutritional aspects of cancer care from the perspective of the medical oncologist.

Methods: A panel of medical oncologists agreed on a series of statements supported by scientific evidence and expert clinical opinion.

Findings: Participating experts emphasized that both poor nutritional intake and metabolic alterations underlie cancer-related malnutrition. The use of liquid and high energy-dense oral nutritional supplements may enable better patient compliance, whereas higher efficacy is more likely with the use of pharmaconutrient-enriched oral nutritional supplements in terms of improved weight, lean body mass, functional status, and quality of life, as well as better tolerance to antineoplastic treatment. A multimodal approach is currently believed to be the best option to counteract the catabolism leading to cancer-related malnutrition; this treatment is scheduled in parallel with anticancer therapies and includes nutritional interventions, multitarget drug therapies, and exercise and rehabilitation programs. Participating experts emphasized the role of the oncologist as a reference professional figure in the coordination of nutritional care for patients with cancer within the context of complex and different clinical scenarios, particularly for permissive-adjunctive nutritional support.

Implications: This review article provides practical guidance addressing major nutritional aspects of cancer care from the medical oncologist's perspective. Thus, this document is expected to assist oncology practitioners in terms of awareness of advances in the nutritional aspects of cancer care and translation of this information into their clinical practice to effectively couple oncologic and nutritional approaches as part of the continuum of care for patients with cancer.

Keywords: Cancer cachexia; cancer patients; medical oncologist's perspective; nutritional screening; nutritional support; treatment.