Clinical Research Support Center

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General Summary

The Clinical Research Support Center was founded in April 2014 to promote the proper conduct of clinical research. The center has the following functions: protocol planning, statistical analysis, data management, monitoring, support for clinical research conduct, and education. We started consulting for clinical research in September 2014 and had 64 protocols of consultation from April 2018 through March 2019. The number of protocols the center consulted on was as follows: research planning, 16; protocol planning and statistics, 25; protocol for randomization/allocation/concealment of emergency key, 4; statistical analyses, 24; preparation of articles, 10; response to reviewers after the submission of articles (including additional analyses), 5; application for the Agency for Medical Research and Development or the Ministry of Education, Culture, Sports, Science and Technology, 10; transition to specified clinical research, 5; and conducting statistical analysis, 7. Consultations were requested by the Departments of Endoscopy, Otorhinolaryngology, Biochemistry, Urology, Neurosurgery, Clinical Oncology/Hematology, Surgery, Orthopaedic Surgery, Anesthesiology, Rehabilitation Medicine, Psychiatry, Cardiovascular Surgery, Pediatrics, Radiology, Breast Endocrinology Surgery, Obstetrics and Gynecology, Pathology, and Emergency Medicine; the Research Center for Medical Sciences; and by the Divisions of Nephrology and Hypertension, Digestive Surgery, Gastroenterology and Hepatology, Regenerative Medicine, Neurology, Respiratory Diseases, and Diabetes, Metabolism and Endocrinology.

In cooperation with the Division of Clinical Pharmacology and Therapeutics we held a "Clinical Trial Seminar" to improve literacy about clinical trials among researchers. The theme was "Big data in cardiovascular diseases and the Clinical Innovation Network" (October 2018). We also held a "Biostatistics Seminar for Tomorrow" consisting of 2 basic courses and 1 advanced course to promote appropriate trial designs and the application of biostatistical methods.

Ethical guidelines for medical and health research involving human subjects have been implemented since April 2015. In addition, the Clinical Trials Act has been enforced since April 2018, after which a certified review board was established at The Jikei University. To meet these requirements, we prepared common forms of protocol, an informed consent form, a standard operating procedure for monitoring, and other documents. For monitoring, clinical research coordinators supported investigators to conduct clinical trials properly.

We introduced a clinical research liaison system to facilitate clinical research. We requested departments that are conducting many clinical trials to assign liaison physicians. Liaison physicians are invited to participate with priority in the "Biostatistics Seminar for Tomorrow" and are expected to act as liaisons between departments to which they

belong and the Clinical Research Support Center.
As a measure against disasters, a clinical data extraction system from electronic health records was introduced in the 4 affiliated hospitals of The Jikei University by using the Standardized Structured Medical record Information eXchange (SS-MIX). We have started to establish a disease registry based on this system in cooperation with medical departments.

Research Activities

Owing to the nature of our center, we collaborate with researchers to conduct various types of clinical studies. In cooperation with the Division of Diabetes, Metabolism and Endocrinology, Department of Internal Medicine, we showed that HbA1c, blood pressure, the body mass index, body weight, and levels of high-density and low-density lipoprotein cholesterol have certain circannual rhythms in patients with type 2 diabetes. Evaluating the variability or absolute value of HbA1c, taking circannual rhythms into consideration, will likely improve the accuracy and precision of risk prediction. However, measuring HbA1c every month in general practice seems difficult because of medical costs.
In our research, we designed population pharmacodynamics models in patients with type 2 diabetes with sparse sampling data to reflect circannual rhythms under real world conditions. As part of the Japan Diabetes Clinical Data Management Study Group, we used patient records from scientific activities to create and validate a model.

Publications

Kuwabara J[1], Kuwahara K[2], Kuwabara Y[1], Yasuno S, Nakagawa Y[1], Ueshima K[1], Kimura T[1] ([1]Kyoto Univ, [2]Shinsyu Univ). Cross-sectional study of the association between day-to-day home blood pressure variability and visceral fat area measured using the dual impedance method. *PLoS One.* 2018; **13:** e0206945.
Liu J[1], Yasuno S, Oba K[2], Konda M[1], Ichihara C[1], Kitao H[1], Kuwabara Y[1], Ueshima K[1] ([1]Kyoto Univ, [2]Tokyo Univ). Long-term effects of antihypertensive therapy on cardiovascular events and new-onset diabetes mellitus in high-risk hypertensive patients in Japan. *J Hypertens.* 2018; **36:** 1921-8.
Nakao YM[1], Miyamoto Y[1], Ueshima K[2], Nakao K[1], Nakai M, Nishimura K[1], Yasuno S, Hosoda K[1], Ogawa Y[3], Itoh H[4], Ogawa H[1], Kangawa K[1], Nakao K[2] ([1]National Cardiovascular Center, [2]Kyoto Univ, [3]Kyusyu Univ, [4]Keio Univ). Effectiveness of nationwide screening and lifestyle intervention for abdominal obesity and cardiometabolic risks in Japan: The metabolic syndrome and comprehensive lifestyle intervention study on nationwide database in Japan (MetS ACTION-J study). *PLoS One.* 2018; **13:** e0190862.
Koda M[1,2], Hanaoka H[3], Sato T[3], Fujii Y[3], Hanawa M[3], Takahashi S, Furuya T[2], Ijima Y[2], Saito J[2], Kitamura M[2], Ohtori S[2], Matsumoto Y[1], Abe T[1], Watanabe K[4], Hirano T[4], Ohashi M[4], Shoji H[4], Mizouchi T[4], Takahashi I[4], Kawahara N[5], Kawaguchi M[5], Orita Y[5], Sasamoto T[5], Yoshioka M[5], Fujii M[5], Yonezawa K[5], Soma D[5], Taneichi H[6], Takeuchi D[6], Inami S[6], Moridaira H[6], Ueda H[6], Asano F[6], Shibao Y[6], Aita I[7], Takeuchi Y[7], Mimura M[8], Shimbo J[8], Someya Y[8], Ikenoue S[8], Sameda H[8], Takase K[8], Ikeda Y[9], Nakajima F[9], Hashimoto M[9], Ozawa T[9], Hasue F[10], Fujiyoshi T[10], Kamiya K[10], Watanabe M[11], Katoh H[11], Matsuyama Y[12], Yamamoto Y[12], Togawa D[12], Hasegawa T[12], Kobayashi S[12], Yoshida G[12], Oe S[12], Banno T[12], Arima H[12], Akeda K[13], Kawamoto E[13], Imai H[13], Sakakibara T[13], Sudo A[13], Ito Y[14], Kikuchi T[14], Osaki S[14], Tanaka N[15], Nakanishi K[15], Kamei N[15], Kotaka S[15], Baba H[16], Okudaira T[16], Konishi H[16], Yamaguchi T[16], Ito K[17], Katayama Y[17], Matsumoto T[17], Matsumoto T[17], Idota M[17], Kanno H[18], Aizawa T[18], Hashimoto K[18], Eto T[18], Sugaya T[18], Matsuda M[18], Fushimi K[19], Nozawa S[19], Iwai C[19], Taguchi T[20], Kanchiku T[20], Suzuki H[20], Nishida N[20], Funaba M[20], Yamazaki M[1] ([1]Univ of Tsukuba, [2]Chiba Univ, [3]Chiba Univ Hospital, [4]Niigata Univ, [5]Kanazawa Medical Univ, [6]Dokkyo Medical Univ, [7]Tsukuba Medical Center, [8]Funabashi Municipal Medical Center, [9]Chiba Rosai Hospital, [10]Kimitsu Chuo

Hospital, [11]***Tokai Univ,*** [12]***Hamamatsu Univ,*** [13]***Mie Univ*** [14]***Kobe Red Cross Hospital,*** [15]***Hiroshima Univ,*** [16]***Nagasaki Rosai Hospital,*** [17]***Chubu Rosai Hospital,*** [18]***Tohoku Univ,*** [19]***Gifu Univ,*** [20]***Yamaguchi Univ).*** Study protocol for the G-SPIRIT trial: a randomized placebo-controlled, double-blinded phase III trial of granulocyte colony-stimulating factor-mediated neuroprotection for acute spinal cord injury. *BMJ Open.* 2018; **8:** e019083.

Fujita M[1]***, Sugiyama M***[2]***, Sato Y***[1]***, Nagashima K***[1]***, Takahashi S, Mizokami M***[2]***, Hata A***[1] ***(***[1]***Chiba Univ,*** [2]***National Center for Global Health and Medicine).*** Hepatitis B virus reactivation in patients with rheumatoid arthritis: Analysis of the National Database of Japan. *J Viral Hepat.* 2018; **25:** 1312-20. Epub 2018 Jun 13.

Sato Y[1]***, Akagi R***[1]***, Akatsu Y***[2]***, Matsuura Y***[1]***, Takahashi S, Yamaguchi S***[1]***, Enomoto T***[1]***, Nakagawa R***[1]***, Hoshi H***[1]***, Sasaki T***[1]***, Kimura S***[1]***, Ogawa Y***[1]***, Sadamasu A***[1]***, Ohtori S***[1]***, Sasho T***[1] ***(***[1]***Chiba Univ,*** [2]***Toho University Sakura Medical Center).*** The effect of femoral bone tunnel configuration on tendon-bone healing in an anterior cruciate ligament reconstruction. *Bone Joint Res.* 2018; **7:** 327-35.

Fujita M[1]***, Sato Y***[1]***, Nagashima K***[1]***, Takahashi S, Hata A***[1] ***(***[1]***Chiba Univ).*** Medical costs attributable to overweight and obesity in Japanese individuals. *Obes Res Clin Pract.* 2018; **12:** 479-84. Epub 2018 Jun 22.

Goda K, Fujisaki J[1]***, Ishihara R***[2]***, Takeuchi M***[3]***, Takahashi A***[4]***, Takaki Y***[5]***, Hirasawa D***[6]***, Momma K***[7]***, Amano Y***[8]***, Yagi K***[9]***, Furuhashi H, Shimizu T***[1]***, Kanesaka T***[2] ***, Hashimoto S***[10]***, Ono Y***[11]***, Yamagata T***[12]***, Fujiwara J***[7]***, Azumi T***[13]***, Nishikawa M, Watanabe G***[14]***, Ohkura Y***[15]***, Oyama T***[4] ***(***[1]***Japanese Foundation for Cancer Research, Cancer Institute Hospital,*** [2]***International Cancer Institute,*** [3]***Nagaoka Red Cross Hospital,*** [4]***Saku Central Hospital Advanced Care Center,*** [5]***Ashiya Central Hospital,*** [6]***Sendai Kousei Hospital,*** [7]***Tokyo Metropolitan Cancer and Infectious Disease Center Komagome Hospital,*** [8]***New Tokyo Hospital,*** [9]***Niigata University Medical and Dental Hospital,*** [10]***Niigata University,*** [11]***Fukuoka University Chikushi Hospital,*** [12]***Sendai City Medical Center,*** [13]***International University of Health and Welfare Ichikawa Hospital,*** [14]***Niigata Cancer Center Hospital,*** [15]***Pathology and Cytology Center).*** Newly developed magnifying endoscopic classification of the Japan Esophageal Society to identify superficial Barrett's esophagus-related neoplasms. *Esophagus.* 2018; **15:** 153-9.