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REVIEW ARTICLE

CRDC: a Chinese rheumatology research platform

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Abstract This review introduces the history of development, organizational structure, funding resources, data collection, and quality control of the Chinese Rheumatism Data Center (CRDC) and summarizes the collection of data. In 2009, Peking Union Medical College Hospital (PUMCH), together with several rheumatism centers, established the Chinese Systemic Lupus Erythematosus (SLE) Treatment and Research Group (CSTAR) to collect data on Chinese patients for the study of SLE disease characteristics. In 2011, CSTAR was extended with the formation of the CRDC at PUMCH with direction from the National Health and Family Planning Commission of the PRC. The CRDC currently includes 300 registration sites and 50 regional sites that have successively begun to collect data on 12 rheumatic diseases, including systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), ankylosing spondylitis (AS), systemic sclerosis, dermatomyositis, Takayasu arteritis, IgG4-related diseases, ANCA-associated vasculitis, gout, polyarteritis nodosa, unclassified systemic vasculitis, and Behcet disease. To date, 17,224 patients have been enrolled in the CRDC. Based on the SLE patients registered in the CRDC, papers investigating basic demographic characteristics and first symptom in Chinese SLE patients, risk factors of pulmonary hypertension, correlations between autoantibodies and clinical manifestations, and factors related to fetal loss have been published. The CRDC is a national registry that provides real-life data to improve clinical decision-making. At the same time, without additional work for the clinician, the CRDC is a powerful research database. The CRDC database provides sufficient information for Chinese clinical studies on rheumatology. Moreover, a mobile device application ensures convenient and efficient data collection without compromising data quality, thereby providing strong evidence-based data for the diagnosis and treatment of Chinese rheumatic patients.

Keywords Clinical registration · Database · Observational study · Systemic lupus erythematosus

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Introduction

Records of patients with rheumatic diseases in real clinical situations, including demographic characteristics, diagnosis, treatment, and clinical information, are essential for clinical studies, which may impact clinical decisions. The clinical database collects the healthcare information of patients in different regions with different diseases, analyzes the key procedures during the treatment process, and provides solutions to problems in clinical practice. Currently, a number of databases for rheumatology have been established worldwide. The Central Finland Rheumatoid Arthritis (RA) database was established in January 1993 and includes demographic measures, treatments, and outcomes of all patients with RA observed in clinics [1]. The STURE database collects efficacy and safety data for all patients beginning biological treatments at the major hospitals in Stockholm as part of the nationwide registry of Antirheumatic Therapies in Sweden [2]. The Oslo approach was to establish a registry of all patients with RA diagnosed according to the American College of Rheumatology (ACR) criteria and to perform follow-up studies of selected cohorts of patients [3]. Since 2000, Danish

rheumatologists have been collecting data on a routine basis in the nationwide DANBIO registry, which includes all rheumatologic patients receiving biological drugs [4]. BioTRAC is an ongoing, prospective registry of patients initiating treatment for RA, ankylosing spondylitis (AS), or PsA with infliximab or golimumab in Canada.

As more rheumatologists plunge into the study of rheumatism and immunological diseases, rheumatology practices are rapidly developing in China. However, many issues still exist in rheumatology in China, such as unbalanced development and a lack of a unified standard in clinical treatment. Therefore, diagnosis and treatment standards for Chinese patients are needed to guide physicians in clinical practice and ensure better care for patients with rheumatic diseases. After receiving financial support from the National Science and Technology Support Project in 2009, Peking Union Medical College Hospital (PUMCH) launched the Chinese Systemic Lupus Erythematosus (SLE) Treatment and Research Group (CSTAR), initiated the research and development of the Chinese SLE Information System (CSIS) in collaboration with several other rheumatology centers in China, and established the national SLE registration standard and information-sharing mechanism among CSTAR members for follow-up and referral of patients to ensure the sustainability of research cohorts [5].

In 2011, the Chinese Rheumatology Data Center (CRDC), a clinical research and translational medicine platform based on CSTAR, was established by PUMCH under the aegis of the National Health and Family Planning Commission of the PRC. Grounded in the developments made by CSIS, the Chinese Rheumatology Information System (CRIS) took shape in service to CRDC when CSTAR completed its remit to collect data on 12 rheumatic diseases, including systemic lupus erythematosus (SLE), RA, AS, systemic sclerosis, dermatomyositis, Takayasu arteritis, IgG4-related diseases, ANCA-associated vasculitis, gout, polyarteritis nodosa, unclassified systemic vasculitis, and Behcet disease. Since 2012, by employing opportunities available as a result of the national "Twelfth Five-year Plan Period" of the 863 program, CRDC expanded the number of registration sites to 300 and the number of regional sites (with Biobank) to 50 based on the standardized construction of regional sites and the Chinese Rheumatology Biobank Platform (CROP).

Methods

Organizational structure and funding sources

As a multi-center, cooperative organization, CRDC has established several professional teams to support its daily operation under the guidance of the CRDC Execution Committee to ensure a sustained and scientific development: (1) CRDC Secretariat—a communication and coordination team for all centers, responsible for organizing clinical training, academic forums, and the communication platform; (2) CRDC IT Department—responsible for the development and maintenance of the information platform; (3) CRDC Data Analysis Department (under construction)—conducts data analysis and reporting and extended data mining. PUMCH scientists in the department of rheumatology and clinical immunology constitute the core operation team and implement tasks efficiently with the collaborative efforts and contributions of supporting teams.

The 300 registration sites accumulate data and samples based on CRDC's single disease inclusion criteria and evaluation procedures in accordance with each center's specific demand. On this basis, regional sites are developed to participate in and complete research projects of the CRDC. Currently, 50 regional sites exist in China and are rapidly developing into the recognized clinical research and referral centers for rheumatology in China.

Supporting sources of funding for the CRDC include research projects at the national and corporate level. Both national and some corporate research projects are conducted through the CRDC platform. To ensure data quality, consistency, and unbiased reporting, sponsors refrain from intervention at the point of data collection for the CRDC platform.

Data collection

Currently, data collection is primarily through handwritten medical records uploaded to the CRIS. All 300 registration sites and 50 regional sites are able to access and import data to the CRIS. At present, 12 types of conditions are included in the CRIS, including systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), ankylosing spondylitis (AS), systemic sclerosis, dermatomyositis, Takayasu arteritis, IgG4-related diseases, ANCA-associated vasculitis, gout, polyarteritis nodosa, unclassified systemic vasculitis, and Behcet disease. Taking SLE as an example, the collected data includes patients' demographic information, medical histories, laboratory examinations, diagnosis, evaluation, treatments, and adverse events. The core dataset of SLE patients is shown in Table 1 [6, 7]. Scheduled visits to patients are conducted in accordance with disease type and patient status with at least one randomized visit every 6 months for the purpose of revealing any anomalous data not otherwise presented.

Data quality control

Measures to control the quality of the electronic information system:

(1) Quality control should proceed in a logical manner to reduce the possibility of handwritten errors. For

Table 1 Core dataset of SLE patients

Diagnosis confirmation
1997 ACR Classification Criteria or 2009 SLICC Classification Criteria
Medical history
Onset time
Diagnosis time
Abnormal reproductive history
Medical history
Family history of rheumatology
Laboratory results
WBC/Hb/PLT/C3/C4/ANA
Anti-dsDNA/Anti-Sm/Anti-RNP/Anti-SSA/Anti-SSB/Anti-rRNP/ACL/Anti-β2GPI/LA
Evaluation
SLEDAI score
Adverse events
Treatment regimen

example, it is not permitted to input menstrual and fertility history for male patients. Abnormal details can be entered with permission when an abnormal examination result exits. For the BILAG index, the assessment will be checked if the evaluation time is ticked. Treatment regimen entries automatically show the common dosage and method of administration for each specific drug.

(2) Results are calculated automatically by the system, including evaluation results, such as BILAG, SLEDAI, and DAS28, to avoid any manual calculation errors.

(3) Quality inspection and feedback are conducted by a professional third-party quality control team.

Ethical and legal considerations

The CRDC collects patient information in full compliance with Chinese laws and regulations on the premise that patients voluntarily agree to their data being collected and sign an informed consent form (ICF). The patients' private information is stored in an encrypted database, as only the attending doctor and patient have the right to review that information.

Results

Currently, 17,224 patients have been enrolled in the CRDC (Fig. 1), of which RA patients are the most common followed by SLE patients (Fig. 2). Based on the SLE patients registered in the CRDC, papers on basic demographic characteristics and first symptom in Chinese SLE patients [5], risk factors of pulmonary hypertension [8], correlations between autoantibodies and clinical manifestations [9], and factors related to fetal loss [10] have been published. The SLE patients in the study of Li et al. showed differing primary symptoms [5], of which rash, arthritis, fever, cytopenia, and kidney disease were the most common. Comparisons of clinical phenotypes in different cohorts are shown in Table 2 [11–15]. Among 1956 patients with complete records of treatment information, 97.4 % received glucocorticosteroid treatment. The pulse therapy dosage was 500 or 1000 mg/day, and the high steroid dose was prednisone >40 mg/day. The proportions of patients receiving different steroid doses are summarized in Fig. 3. The number of patients receiving an immunosuppressant alone was 51 (2.6 %). The proportions of patients receiving various immunosuppressants are shown in Fig. 4.

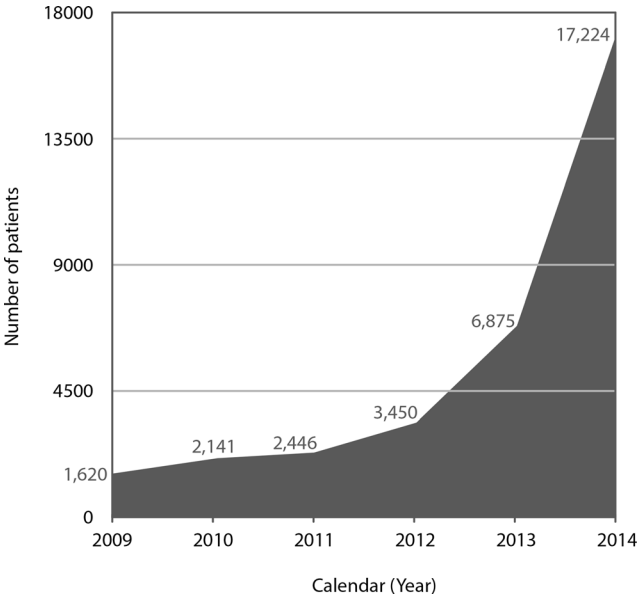

Fig. 1 The accumulated number of patients in the CRDC

As the CRDC has gradually developed into an information-sharing platform for scholars conducting clinical studies on rheumatology and a basic research application, many relevant

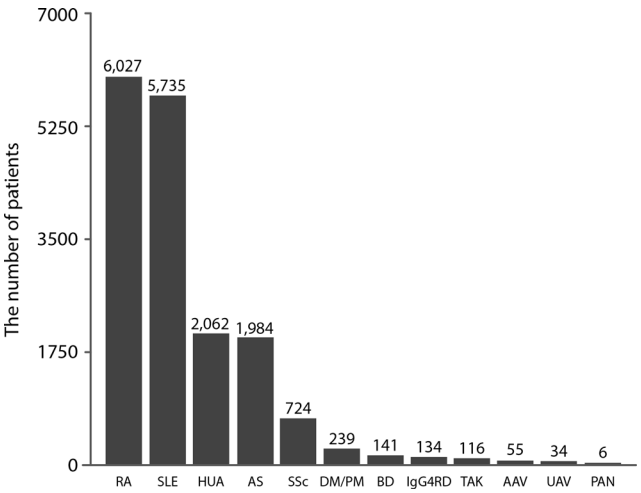

Fig. 2 The numbers of patients with the 12 different diseases registered in the CRDC

Table 2 Comparison of cumulative main characteristics (%) related to SLE in several large cohorts

Author	Petri, et al. [11]	Wang, et al. [12]	Alarcón, et al. [13]	Cervera, et al. [14]	Pons-Estel, et al. [15]	CSTAR
Number of patients	574	539	555	1000	1214	2104
Geographical area	USA	Asia, Malaysia	USA	Europe	Latin America	Asia, China
Malar rash	331(57.7)	410(76.1)	322(58)	311(31.1)	744(61.3)	1009(47.9)
Discoid lesions	162 (28.2)	30(5.6)	107(19.3)	78(7.8)	143(11.8)	118(5.6)
Photosensitivity	335(58.4)	222(41.2)	334(60.2)	229(22.9)	681(56.1)	526(25.0)
Oral ulcers	219(38.2)	185(34.3)	293(52.8)	125(12.5)	506(41.7)	466(22.1)
Arthritis	NR	272(50.5)	489(88.1)	481(48.1)	NR	1147(54.5)
Serositis	NR	108(20)	287(51.7)	160(16)	268(22.1)	345(16.4)
Hematologic involvement	NR	263(48.8)	404(72.8)	182(18.2)	880(72.5)	1181(56.1)
Nephropathy	319 (55.6)	399(74)	223(40.2)	279(27.9)	628(51.7)	998(47.4)
Neurologic involvement	NR	123(22.8)	67(12.1)	194(19.4)	321(26.4)	101(4.8)
ANA	NR	500(92.8)	538(96.9)	NR	1137/1161(97.9)	2063(98.1)

NR not reported

research projects have been able to make effective use of data available through this platform: (1) the study on clinical diagnosis and comprehensive treatment of SLE (Project No. 2008BAI59B02), a Key Project in the National Science & Technology Pillar Program in the "Eleventh Five-year Plan Period"; (2) the molecular subtyping and individualized treatment technology of SLE (Project No.2012AA02A513), a Project of the National High-Tech R&D Program (863 Program) in the "Twelfth Five-year Plan Period"; (3) the registration study of desmosis-related pulmonary hypertension in the study of the disease of pulmonary circulation and cardiac function (Project No. 2011BAI11B15), a Key Project in the National Science & Technology Pillar Program in the "Twelfth Five-year Plan Period"; (4) the national database of the registration of rheumatology, a Project in the National Science & Technology Infrastructure Platform; (5) the project of standardized diagnosis and treatment of rheumatoid arthritis in China (CREATIVE), a Project by the Department of Medical Administration in the MOH; (6) the China Center project of the EULAR Scleroderma Trials and Research group (EUSTAR); (7) the registration study of Bosentan SLE/systemic sclerosis-related pulmonary hypertension (PAH) in China; (8) the standardized diagnosis and treatment of ankylosing spondylitis (AS) and the registration study of adalimumab AS; (9) the study on the mechanism and control strategy of ankylosing spondylitis (Project No.2014CB541800), a National "973" Program; (10) the early diagnosis and intervention of atherosclerosis praecox in patients with SLE, a special clinical medicine project approved by Beijing Municipal Science and Technology Commission; (11) the multi-center online registration and follow-up study on patients with gout and hyperuricemia; and (12) the study on the diagnosis of RA molecular subtype, a study on standardized diagnosis and treatment of key diseases approved by the Science and Technology Office of Jiangsu province; and other investigator-initiated studies.

Discussion

As the first rheumatology data center in China, the CRDC provides abundant information for clinical studies of Chinese rheumatic patients. Compared to the existing rheumatology databases worldwide, the CRDC collects information on more types of diseases and enrolls more patients; thus,

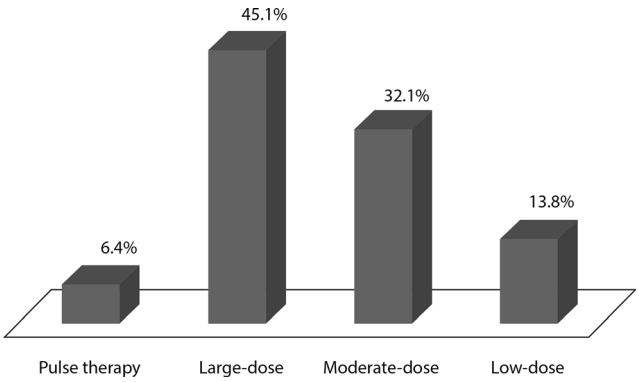

Fig. 3 Proportions of patients by dose of glucocorticosteroid

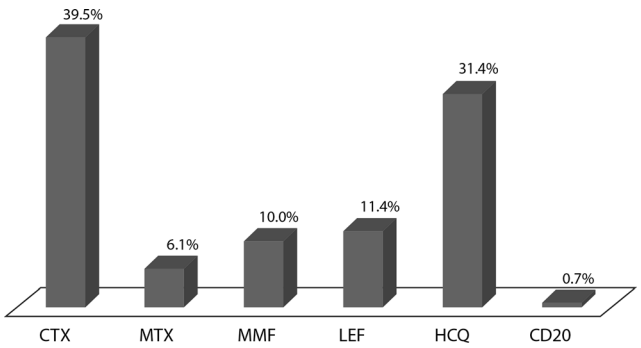

Fig. 4 Proportions of patients by various immunosuppressants

it can be used for larger-scale clinical research projects. Access to information on rheumatism patients from different regions and hospitals at different levels enables rheumatologists to perform detailed analyses for diagnosis and treatment processes, to understand the correlations between diagnosis, treatment, efficacy and cost, and to find disparities and their causes and identify difficult problems. Thus, rheumatologists can optimize the diagnosis and treatment processes by utilizing the CRDC. The CRDC also expands rheumatologists' knowledge of risk factors, inducing factors, and clinical morbidities and manifestations of rheumatism in China.

The basic demographic characteristics of SLE patients in China are congruent with international data. Up to 97.4 % of the SLE patients was subjected to steroid therapy, the majority of whom were given high-dose therapies, and this may be associated with the baseline disease activity in these patients. These results will be helpful in the diagnosis of SLE in Chinese patients and provide medical evidence for subsequent treatment.

To better integrate the clinical diagnosis and treatment process and optimize it to achieve a more effective combination of data and scientific research, the CRDC has developed a mobile terminal and initiated its application. The technical characteristics of the mobile terminal has solved issues with the outpatient system and wards' network capabilities due to their installed communication equipment. The mobile terminal also allows patient profiles to be managed uniformly by printing standardized medical records using Wi-Fi-connected printers and has increased clinical efficiency and quality by implementing patient self-reports and self-evaluation forms in advance of treatment. The mobile terminals not only assist in scientific research do to their powerful and professional CRIP system but also play a key role in increasing the efficiency of clinical practice, thereby, creating a better clinical environment and improving the relationships between doctors and patients.

The CRDC will continue to follow the principle of "sharing information and prioritizing contributions" and to endeavor to implement the multi-center study of rheumatology in China by establishing the following: (1) the data standardization and sharing mechanism of the national rheumatology data management platform; (2) the sampling standardization and cooperative mechanism of the national rheumatology biological sample platform; (3) the robust evaluation and improvement mechanism of the national rheumatology quality control platform; (4) the feedback normalization and authentication mechanism of the national rheumatology continuing education platform; and (5) the direct reporting and monitoring mechanism of the national rheumatology and other chronic diseases management platform. The CRDC is dedicated to becoming an internationally recognized brand in rheumatology through increased international cooperation.

Conclusions

The CRDC provides sufficient information for Chinese clinical studies examining rheumatology. Moreover, a mobile device application for the CRDC ensures convenient and efficient data collection without compromising data quality, thus, providing strong evidence-based data for the diagnosis and treatment of Chinese rheumatic patients.

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Disclosures None.

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