Research Square

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Registration of Rectal Cancer-Related Clinical Trials on Chinese Clinical Trial Registry over past decades

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Research

Keywords: Rectal cancer, Clinical trials, Chinese Clinical Trial Registry

Posted Date: February 12th, 2020

DOI: https://doi.org/10.21203/rs.2.23371/v1

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Abstract

Background This study investigated and analyzed rectal cancer-related clinical trials registered on Chinese Clinical Trial Registry (Chi-CTR) by the end of 2018. We aimed to discuss the characteristics and developmental trends.

Methods The Chi-CTR database was searched and all clinical trials related to rectal cancer extracted. The time limit for the search was from the establishment of the data library to December 31, 2018. The characteristics of registered clinical trials were then analyzed.

Results A total of 70 clinical trials were retreived. Beijing, Shandong, and Guangzhou accounted for 47.1% of the total number of registered clinical trials. Sichuan and Sun Yat-sen Universities having the highest number of registrations. The registration status of the 55 trials was prospective registration. The top sources of funding were self-financing (41.4%), hospital funding (22.9%) and local finance (15.7%). Out of the 43 randomized controlled trials, 39 were either blank or missing in the blinded section. The sample size of clinical trials was high in 100 to 199 cases. Only eight of the 70 trials were multicenter clinical trials.

Conclusions Relevant departments should increase the registration of clinical trials, increase the awareness of registration, and promote the development of high-quality clinical trials. At the same time, researchers should raise the awareness of clinical trial registration, and actively carry out multi-center clinical trials.

Background

Rectal cancer is one of the most common cancers globally [1, 2]. In China, its prevalence ranks 4th and 5th among the females and males, respectively [3]. The economic burden of rectal cancer is likely to increase in China due to the rising population of the aged and adoption of Western lifestyle [4]. Presently, treatment of rectal cancer follows a multidisciplinary comprehensive treatment approach involving surgery, radiotherapy, chemotherapy and targeted therapy [5].

A clinical trial involves administration of one or more health-related interventions to participants or populations to assess the efficacy. Clinical trials have to be registered first, before their implementation [6]. In May 2006, the world health organization (WHO) officially launched the International Clinical Trials Registry Platform (ICTRP), which is a key measure to achieving transparency, data sharing and improved quality of Clinical Trials [7]. The International Committee of Medical Journal Editors (ICMJE) requires all clinical trials to be registered internationally before their results are published[8]. The Chinese clinical trial registry (Chi-CTR) was the first to be certified by ICTRP in 2007 to register clinical trials not only in China but also globally.

A clinical trial is a powerful tool widely used in rectal cancer research to explore the diagnosis, prevention and treatment of rectal cancer. We analyzed the Chi-CTR database for all rectal cancer related clinical

trials, to establish the current situation and assess the trend in clinical trial registration in China.

Methods

1 Eligibility criteria

All clinical trials related to prevention, treatment, and prognosis of rectal cancer, were included in this study, regardless of design or completion.

2 Search

The term "cancer" was searched in the Chi-CTR database (http://www.chictr.org.cn/) and all the rectal cancer related trials retrieved until December 31, 2018.

3 Data extraction

Two researchers independently screened the Chi-CTR database and extracted relevant data, which was later cross-checked. Disagreements were resolved through discussion or consultation with a third party. The clinical trials and the data content to be extracted for this study were determined by consensus after reviewing all related clinical trials. The data extracted included: (1) Basic information of the registered research; research topic, registration status, time of registration, institution, region, etc.; (2) Sources of research funding; (3) Type of research and design scheme;(4) register the relevant characteristics of the study.

4 Data analysis

Data entry was done in Excel and qualitative data described by frequencies and proportions.

Results

1 Research screening process and results

Out of the 71 registered studies initially examined, 70 which were related to rectal cancer were finally included in the study after verification.

2 Registration time distribution

The first two years (2008 and 2009) recorded the lowest number of registered rectal cancer related clinical trials at one. However, there was gradual increase between 2013 and 2017 as shown in Figure 1.Among 70 trials, 55 trials were prospective registration while 15 were retrospective registration. 19 clinical trials were not scrutinized by the ethics committee.

3 Regional and institutional distribution

Beijing, Guangzhou and Shandong had the highest number of registered rectal cancer related clinical trials, accounting for 47.1% of the total registered trials. On the other hand, Shanxi, Liaoning, Jiangxi, Hunan and Fujian, each had only one registered clinical trial. The regional distribution of registered clinical trial sources is shown in Figure 2. The seven institutions that had three or more registered trials include; Sichuan university (Sichuan), Sun yat-sen university (Guangzhou), Beijing university (Beijing), Qingdao university (Shandong), naval military medical university (Shanghai), Shanghai Jiao tong university (Shanghai) (Zhejiang) and Yangzhou university. The distribution of registered clinical trial sources is shown in Figure 3.

4 Funding sources

Sixty-eight registered clinical trials were funded. The top sources of funds were revealed to be self-financing, hospital funding, local finance and university funding (Table 1).

Table1. Chi-CTR registered funding sources for clinical trials related to rectal cancer

Funding source	Number of records	Percentage of records (%)
Self-funding	29	41.4
Hospital funding	16	22.9
Local finance	12	17.1
University funding	4	5.7
National finance	3	4.3
Business	3	4.3
No funding	2	2.9
Social welfare fund	1	1.4

5 Study types and Study design

Among the clinical trials included in this study, intervention studies were the highest in number (43, 61.4%), followed by observational studies (14, 20%) and diagnostic test studies (9, 12.9%). Preventive, prognostic, and etiology/related factor studies accounted for the remaining 5.7% (Table 2). There were 8 types of study designs which included; randomized controlled trials, diagnostic accuracy of diagnostic trials, before-after controlled studies, continuous cases, cross-sectional studies, case-control studies, non-randomized controlled trials and cohort studies (Table 3).

Table 2. Study types of Chi-CTR registered rectal cancer related clinical trials

Study type	Number(n)	Percentage(%)
Interventional study	43	61.4
Observational study	14	20.0
Diagnostic test	9	12.9
Prevention	2	2.9
Prognosis study	1	1.4
Cause/Relative factors study	1	1.4

Table 3. Study designs of Chi-CTR registered rectal cancer related clinical trials

Study design	Number(n)	Percentage (%)
Randomized controlled trial	43	61.4
Diagnostic test diagnostic accuracy	7	10.0
Pre- and post-control study	7	10.0
Continuous case	3	4.3
Cross-sectional study	3	4.3
Case-control study	3	4.3
Non-randomized controlled trial	2	2.9
Cohort study	2	2.9

6 Feature analysis included in randomized controlled clinical trials

A total of 43 randomized controlled clinical trials were included in feature analysis. Out of these, 26 trials were registered as simple randomized method, followed by nine as computer randomized method, five as block randomized method and two as stratified randomized method (Table 4). There were two

experiments that detailed the allocation concealment process. Using the blind method, only 4 registered clinical trial registrations were blind (9.3%) while 39 were either blank or missing (Table 4).

Table 4. Feature analysis included in randomized controlled clinical trials

Item	Number(n)	Percentage(%)
Random method		
Simple random method	26	60.5
Computer randomization	9	20.9
Block random method	5	11.6
Hierarchical random method	2	4.7
other	1	2.3
Blind method		
Single blind	1	2.3
Double blind	3	7.0
Blank/missing	39	90.7

7 Feature analysis of clinical trials

In the registered clinical trials of rectal cancer in China, 42 clinical studies were labeled as either other or unlabeled by stage. Mark test stage has 28: including period (8) the highest proportion, 11.4%. Among the registered rectal cancer related clinical trials, 62 were from domestic single centers, 7 from domestic multi-centers and one from an international multi-center (Table 5). From the registered clinical trials of rectal cancer in China, the largest number of samples ranged between 100 and 199 (22, 31.4%), as shown in Table 5.

Table 5. Feature analysis of clinical trials

Category	Specifics	Number	Percentage
Study phase			
	0 phase	5	7.1
	I phase	5	7.1
	I-II phase	4	5.7
	II phase	8	11.4
	III phase	1	1.4
	IV phase	5	7.1
	Other	42	60.0
participating center			
	Domestic single center	62	88.6
	Domestic multi-center	7	10
	International multi-center	1	1.4
Sample size			
	<20	9	12.9
	20~49	7	10
	50~99	10	14.3
	100~ 199	22	31.4
	200~ 299	5	7.1
	300 ~ 399	6	8.6
	400 ~ 499	4	5.7
	500~ 999	5	7.1
	≥1000	2	2.9

Discussion

The number of rectal cancer related clinical trials registered on Chi-CTR significantly increased between 2008 and 2017., This is an indication that researchers are gradually beginning to register their clinical trials. Beijing, Shandong and Guangzhou had the highest number of registrations, accounting for 47.1% of the total number of clinical trial registrations for rectal cancer in China. This indicates that there is a regional imbalance in the registration of clinical trial for rectal cancer in China. Clinical trial is a huge and

complicated systematic project, which needs a strong economic guarantee and technical support[9]. Both Beijing and Guangzhou, have developed economies and skilled technical personnel that can easily support development of clinical trials. The number of registered trials in Sichuan university was significantly higher than that in other universities. This could be attributed to the fact that West China hospital of Sichuan university, is the pioneer and main training base of clinical research methodology and evidence-based medicine in China. However, abundance of universities and colleges within a province (city) did not guarantee high number of registrations of rectal cancer related clinical trials, for the region. This could be attributed to the fact that economically developed regions, without university affiliated hospitals, actively participate in the registration of clinical trials. Funding sources were mainly self-finances, hospital funds and local finances. After the trials completion, reports have shown that the rate of sharing data from government-funded clinical trials is relatively high. [10]. Lack of funds is one of the major setbacks in implementation of clinical trials [11]. Countries should therefore strive to support rectal cancer research by allocating funds to it.

Most of the clinical trials related to colon cancer registered in the Chi-CTR database were interventional studies. The interventional studies were all RCTS (randomized controlled trials). RCT has been reported to be an ideal method to test the safety and efficacy of clinical interventions, and its conclusions are of great significance in guiding clinical practice and drug policy [12]. RCT reduces or eliminates the imbalance between the treatment group and the control group, occupies the top of the pyramid of clinical evidence, and is the best source of evidence-based medicine [13]. Randomization is an important principle in RCT where subjects are randomly assigned to the experimental group and the control group to balance the known and unknown confounding factors of the experimental group and the control group. This improves the comparability between the two groups and makes the research findings more reliable [14]. Most of the included RCT adopted the randomization method. Allocation concealment refers to the grouping process after random number sequences are generated, with the purpose of avoiding selectivity bias and improving research quality [15]. However, there are only two experiments that specify allocation concealment process. Blind method is often implemented after the completion of test grouping to avoid implementation bias and measurement bias [16]. Only four of the included studies explicitly reported the use of blind method. Clinical trials that have not been carried out, or have not been carried out in full with randomized, allocation concealment and blind methods lead to bias of results.

In 2012, Savovic et al. [17] used the meta-epidemiological method to quantitatively evaluate the impact of unimplemented or inadequately implemented random, allocation concealment and blind methods on the research results. The bias brought by unimplemented or inadequately implemented blind methods was the revealed to be the largest. Among the registered rectal cancer clinical trials in China, the largest number of clinical trials (22, 31.4%) was between 100 and 199 samples. An adequate sample size is critical in the development of clinical trials. High quality retrospective or prospective studies require a reasonable sample size estimate with the participation of biostatisticians. The sample size estimation should be based on the main endpoint of the study, and the conclusions of the study should also be based on the main endpoint indicators [18]. This study revealed that development of clinical trials had

been done in eight multi-centers in China. Not only can this accelerate the progress of clinical trials but also greatly improve the completion efficiency of the clinical trials. In addition, conclusions from multi-centers can be extrapolated unlike those of single-centers [19].

Clinical trial registration mechanism is an effective method to realize the transparency of clinical trial information and improve the quality of clinical trials [20]. Complete and standardized registration information can effectively improve transparency and promote mutual communication [21]. Clinical trial registration, unbiased reporting of results and sharing of raw data are key components of clinical trial transparency [22]. In addition, the biomedical periodicals need to establish important clinical research policies to promote transparency, improve the quality of research reports, and guide data sharing. Standardized clinical trial registration system and rigorous clinical research methods provide guarantee for the authenticity of clinical trials. It also make implementation of the trials to adhere to rules and regulations, and reduce the impact of all artificial or non-human bias on the authenticity of clinical trials. The main purpose of registration of a clinical trial is to check the quality of clinical medical research evidence at the source, therefore ensuring reasonable use of people's health and health resources [23].

Shortcomings and limitations of this paper: Due to the real-time dynamic changes of information in the clinical trial registration database, the results of this study can only explain the status of rectal cancer related clinical trials registered in Chi-CTR platform by the end of 2018. Therefore, the results do not reflect the status of unregistered studies and also cannot represent the overall level of clinical research on rectal cancer in China.

Conclusion

The numbers of clinical trials related to rectal cancer that were registered in Chi-CTR showed a rising trend and the regional imbalance was also significant. Some researchers have incomplete and irregular data in clinical trial registration. Relevant departments should increase the publicity of clinical trial registration, improve the awareness of registration, and promote the development of high-quality clinical trials. Researchers should carefully study the knowledge of clinical trial registration, improve the awareness of clinical trial standard registration, and actively carry out multi-center clinical research.

Abbreviations

Chi-CTR: Chinese Clinical Trial Registry

WHO: World health organization

ICTRP: International Clinical Trials Registry Platform

ICMJE: International Committee of Medical Journal Editors

Declarations

Ethics approval and consent to participate

Not applicable

Consent for publication

Not applicable

Availability of data and materials

The datasets generated and analyzed during the current study are available in the http://www.chictr.org.cn/

Funding

This work was supported by the Wu Jie Ping Medical Foundation Clinical Research Special Fund [320.2710.1836], the Henan University Graduate Student "talent plan" [SYL18060141], basic research project of key scientific research projects in colleges and universities[17B320003] and key research and development and promotion of special scientific and technological research of Henan [182102310544]. The funders were not involved in the design of the study or the decision to submit the manuscript for publication nor were they involved in aspects of the study conduct. The views expressed in this manuscript are those of the authors and may not be understood or quoted as being made on behalf of, or as reflecting the position of, the funder(s) or any institution.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

S.C.Z. and J.H.H. conceived and designed the project. Q.Z. and X.W.L. collected the data. C.Y.W. and J.J.Z. analyzed and interpreted the data. Z.G. drafted the manuscript. All authors read and approved the final manuscript.

Acknowledgements

Not applicable

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Figures

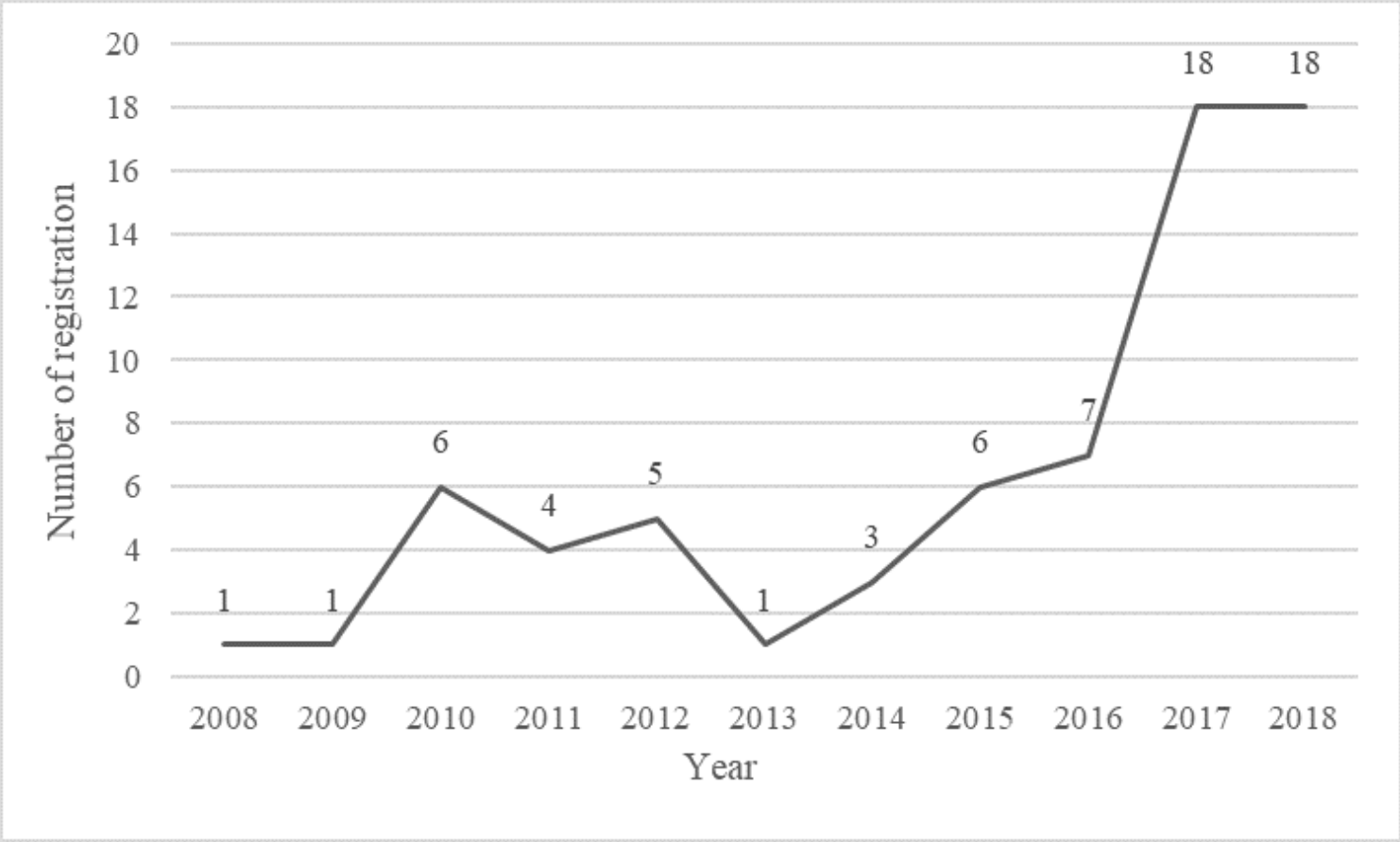

Figure 1

Time distribution of clinical trials of rectal cancer registered in Chi-CTR

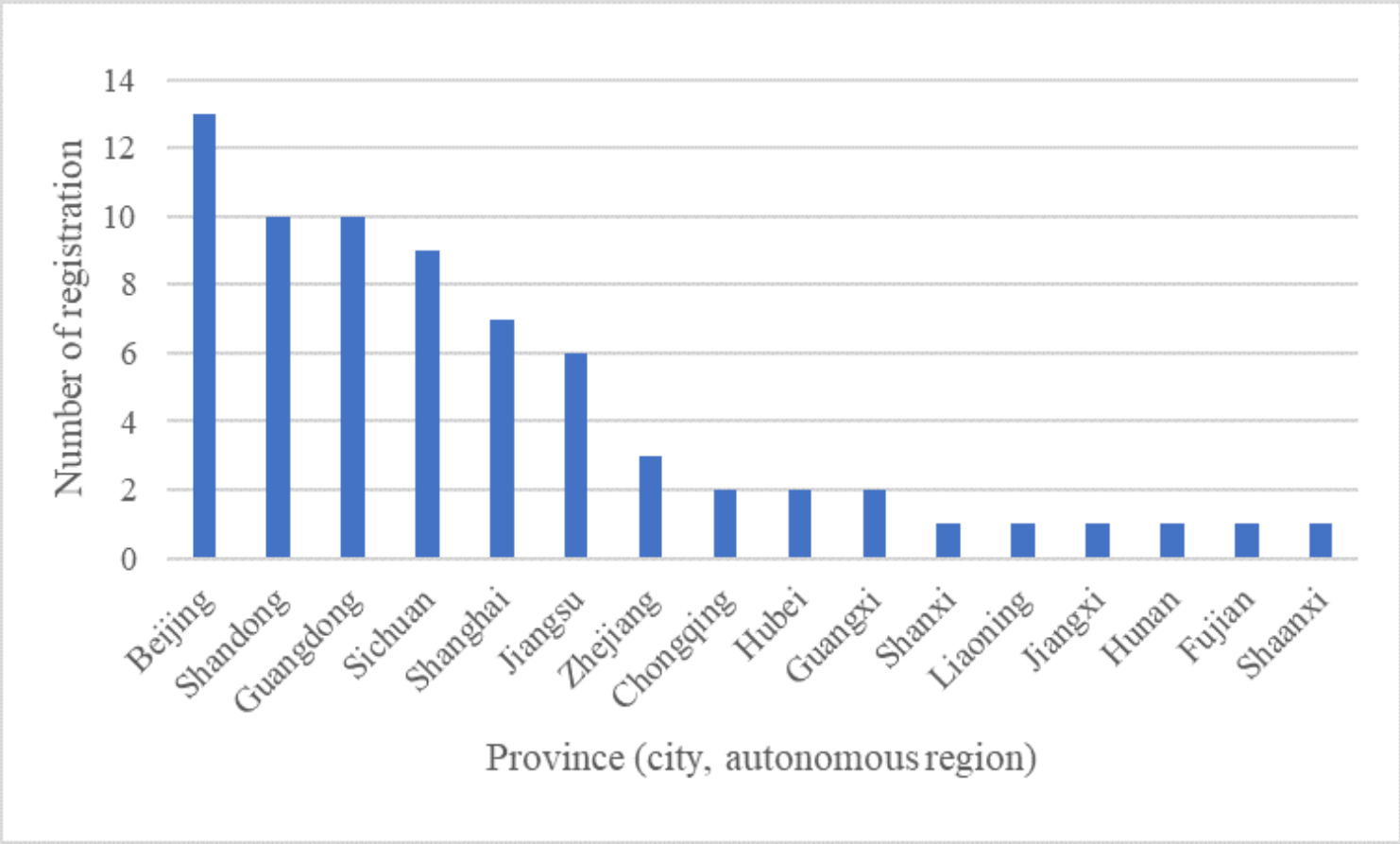

Figure 2

Regional distribution of clinical trials of rectal cancer registered in ChiCTR

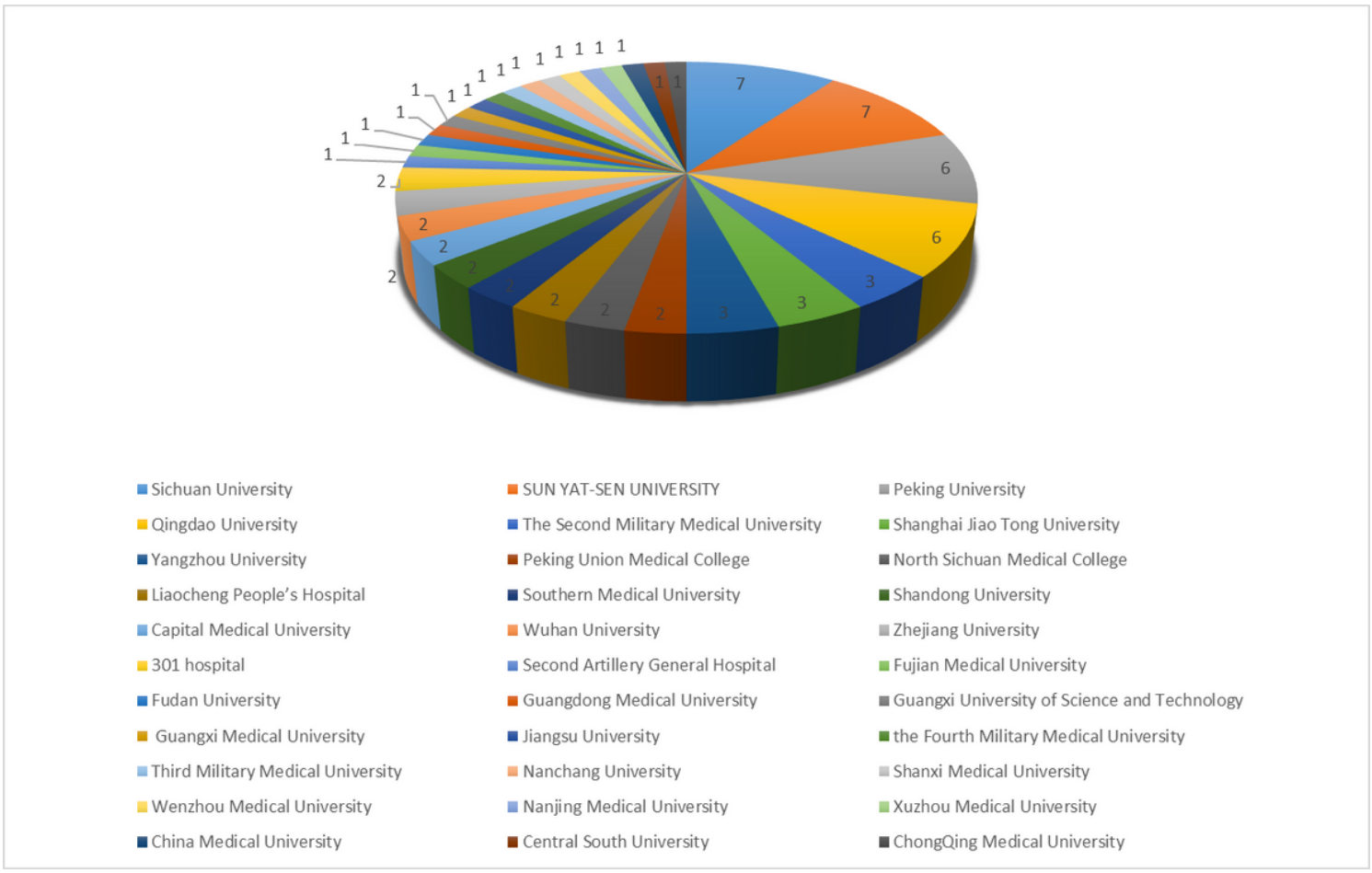

Figure 3

Institutional distribution of Chi-CTR registered rectal cancer related clinical trials

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