

Freeze-all embryo transfer awareness and acceptance of IVF-ET patients in China

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Abstract

The aim of the study was to determine the level of awareness and acceptance of in vitro fertilization pre-embryo transfer (IVF-ET) patients for freeze-all embryo transfer, improve relevant technical specifications, and optimize treatment results based on medical experience.

Questionnaires were completed by women who received in vitro fertilization embryo transfer. A total of 377 valid samples were included into this study. Through focus group discussions and tablet assisted intercept interviews, we analyzed the basic situation, the awareness for frozen-all embryo transfer, and the need for frozen-all embryo transfer information for infertile patients.

In this study, 60% of patients received IVF-ET for the first time, whereas the remaining patients received IVF-ET more than once. We investigated the current awareness and acceptance of IVF-ET patients for freeze-all embryo transfer quantitatively. Patients were grouped based on quantitative measurements, and the mainstream group of patients (72.7%) was precisely the patients who were worried and concerned of frozen-all embryo transfers. Although few of them could “rationally accept the comparative advantage of the technology,” this group was vulnerable to doctors’ guidance and education. Eventually, this group of patients accepted the frozen-all embryo transfer.

Since there are no certain criteria for the kind of embryo transfer patients and reproductive centers should take, the choice should be taken individually according to the social economic situation and acceptance of patients for the frozen embryo transfer, as well as the technology of the reproductive center.

Abbreviations: COS = controlled ovarian stimulation, eFET = elective frozen embryo transfer, ET = embryo transfer, FET = frozen-thawed embryo transfer, IVF-ET = in vitro fertilization pre-embryo transfer, OHSS = ovarian hyperstimulation syndrome.

Keywords: attitude, embryo transfer, IVF-ET, questionnaire

1. Introduction

After the performance of the first clinical pregnancy case of frozen-thawed embryo transfer (FET) in the 1980s,^[1] FET has become an important component of in vitro fertilization embryo transplantation (IVF-ET) technology together with fresh embryo transfer (ET). The risk of severe ovarian hyperstimulation syndrome (OHSS) is decreased when patients with high risk of OHSS receive natural cycle frozen embryo transfers.^[2] Since the

remaining embryos are frozen and stored for future transplantation, the reduction in the number of fresh embryos transferred becomes more acceptable for reducing the possibility of multiple pregnancy.^[3,4] FET is a better technology for patients with certain systemic diseases, cervical tension, stenosis, bleeding, poor endometrial development, or endometrial polyps. These patients are unable to accept embryo transfer. Freezing technology retains the opportunity to continue treatment for patients with certain unexpected social or psychological reasons and cannot accept fresh embryo transplantation. Freezing technology helps patients receiving egg donation treatment in some special cases, such as the lost coordination of cycle synchronization of the donor and acceptor, providing a screening time for the infectious or genetic disease of the donated embryo.^[5,6] Freezing technology also retains the possibility of offspring for patients receiving chemotherapy or radiotherapy. Therefore, patients, for some reason, do not receive fresh embryo transfer and freeze all embryos for future transplants, known as elective frozen embryo transfer (eFET). At present, the main indications of eFET are: to prevent OHSS in patients with ovarian hyperresponsiveness; to accumulate embryos for patients with poor ovarian response; to provide preimplantation genetic diagnosis; the nonsynchronization of endometrium and embryo development. With the continuous development and improvement of technology and clinical experience, the success rate of “test-tube baby” has gradually increase in the world, and these 2 embryo transfer methods both have a good pregnancy rate.^[7,8] However, the definition of success is not limited to pregnancy rate. The ultimate goal is to obtain live births. Compared with ET, many studies have found that FET can reduce the incidence of OHSS,^[2] low birth weight children, small for gestational age

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children, premature birth, low birth weight, premature delivery, placenta previa, placental abruption, antepartum hemorrhage, and perinatal death^[9,14] without reducing pregnancy and live birth rates. Shapiro et al^[15] proposed the implementation of nonselective freeze all embryo transplantation (freeze-all ET); that is, to freeze all embryos after in vitro fertilization, and not a “fresh embryo transfer.”

Clinicians need to adjust their missionary methods, programs, and treatment-related decisions according to the demands and worries of patients. However, there is no large-scale research on the attitudes of patients in selecting an FET technology. This study first investigated these attitudes and its changes after dissemination in infertile patients in Beijing and the surrounding areas. Most patients preferred FET after receiving clinical pregnancy and complications related data, and thought that the clinical data shown by the doctors were more reliable.

2. Materials and methods

This study was conducted in accordance with the declaration of Helsinki. This study was conducted with approval from the Ethics Committee of our hospital. Written informed consent was obtained from all participants.

2.1. Subjects

A total of 377 patients who received IVF-ET therapy at the Center for Reproductive Medicine, the People's Hospital of Peking University from March 6, 2015, to April 8, 2015, were enrolled into this study. All patients provided an informed consent prior to enrollment into this study and completed a questionnaire. Patients without access to receive IVF-ET were excluded from the study.

2.2. Questionnaire and statistics

The tablet assisted questionnaire at the Center for Reproductive Medicine was used as an intercept interview point after focus group discussions. Awareness, acceptance, and attitude changes in degree of advantage after informing the patient about FET were qualitatively collected through focus group discussions, in order to establish a structured quantitative questionnaire design. The questionnaire comprises of 3 parts: the patient's background information, screening questionnaire, and the main questionnaire. SPSS 19.0 software was used for statistical analysis. Cluster analysis was used to classify and analyze the attitudes data.

3. Results

3.1. Patients

The main components of the patients were: 25 to 44 years old, resides in the Beijing area, no children, and mainly middle socio-economic level. Approximately 78.2% of patients were female, whereas the remaining participants were male. As for education, junior college graduates accounted for 75.3%. Half of these patients had a monthly family income of 8000 yuan.

Approximately 89.1% of patients had a duration of infertility of >2 years, whereas 36.6% of patients had a duration of infertility of >5 years. In addition, 49.9% of these patients received IVF-ET therapy.

As for the cost of treatment, 56.2% of patients spent ≤50,000 yuan, 29.7% of patients spent 50,000 to 100,000 yuan, and 14.1% of patients spent >100,000 yuan. Patients who planned to receive IVF-ET at the Center for Reproductive Medicine of the People's

Hospital of Peking University accounted for 98.1%. The reason for this selection was mainly due to the doctor (good reputation of the doctor, 63.1%; the doctor is an expert and famous, 53.6%) and hospital (good reputation of the hospital, 51.7%).

As for the relevant experience aspects of IVF surgery, 60.7% of the patients were at their first attempt, 22% of patients failed in their first time and decided to make a second attempt, and 16.2% of patients had >2 attempts and all attempts failed.

Among the 148 patients who received IVF surgery, ET patients accounted for 35.1%, frozen embryo transfer patients accounted for 33.1%, and patients who received both accounted for 27.7% (Table 1).

3.2. Awareness and access of FET in enrolled patients

For the awareness and implementation of FET: 43.8% of the patients only heard about it, but never implemented it; 40.1% of the patients never heard about it; 16.2% of patients heard about it and implemented it.

Among the 226 patients who heard about FET, the main sources of information were doctors, patient's recommendations, and internet queries (35%, 35%, and 29.2%, respectively).

Among the 165 patients who only heard about it, but never implemented FET: 55.8% of these patients “only heard, but did not understand, and they could not judge which one was better”; 29.1% of these patients “heard about it, did not understand it,

Table 1
Characteristic of enrolled 377 patients.

	N	Percentage (%)
Gender		
Male	82	21.8
Female	295	78.2
Age, y		
18–24	5	1.3
25–29	60	15.9
30–34	143	37.9
35–44	158	41.9
45–54	11	2.9
Infertility history, y		
2–5	198	52.5
≥5	138	36.6
Education background		
Junior college degree or above	284	75.3
Family structure		
≥1 children	23	6.1
No child	354	93.9
Locality		
Beijing	278	73.7
Other regions	99	26.3
Average monthly income		
<8000 yuan	189	50.1
≥8000 yuan	188	49.9
Therapy history		
IVF-ET	188	49.9
Chineses traditional medicine	141	37.4
Combined therapy*	240	63.7
Previous spending on treatment		
<50 thousands yuan	212	56.2
50–100 thousands yuan	112	29.7
≥100 thousands yuan	53	14.1

IVF-ET = in vitro fertilization pre-embryo transfer.

* Combined therapy: patients have received both IVF-ET and Chinese traditional medicine treatment.

and felt that it was not as good as ET”; 15.2% of these patients “heard of the technology, and also had a better understanding of the relative benefits of FET.”

Among the 61 patients who underwent FET before surgery: 42.6% of patients “only heard, but did not understand, and could not judge which one was better”; 19.7% of patients “heard of the technology, and had a better understanding of the relative benefits of FET”; 27.9% of patients “heard about it, did not understand it, and felt that it was not as good as ET”; 8.2% of patients “never heard of it.” Approximately 83.6% of patients who underwent FET were not fit for fresh ET, and underwent FET following doctors’ recommendations, whereas other patients were able to undergo fresh ET, but was convinced by doctors and other patients. The majority of the 61 patients underwent FET at Center for Reproductive Medicine, the People’s Hospital of Peking University (93.4%). Among these patients, ~75.4% of patients “had failed pregnancy or had biochemical pregnancy”; 9.8% of patients “had a successful pregnancy, but had still birth”; 6.6% of patients “had a successful pregnancy, but had spontaneous abortion”; 6.6% of patients “had a successful pregnancy and childbirth”.

3.3. Attitude to FET in enrolled patients

3.3.1. Grouping based on patient attitudes. According to patient views preliminarily obtained through the focus groups, a total of 19 attitude measuring statements were structured. Using the fast clustering method, patients were grouped into the following 3 categories:

The first category is affected mainly by socioeconomic factors (time cost, energy cost, or expense costs), holds a basic negative attitude on FET, was defined as “FET-not-needed patients,” and accounted for 17.5% of the total sample.

The second category had a high score of “socio-economic factors,” and had the highest score for the other 16 measurement statements. In these 16 statements, 6 were used to describe the “rational concerns” of patients for FET technology, 4 were used to describe the “no sense” of patients for FET, 3 were used to describe the anxiety of patients for the technology, and 3 were used to describe the “rational acceptance” of patients. This category not only resulted to rational concerns on the FET technique, but also presented some loss and anxiety. These patients accounted for the highest, reached 72.7% of the total number of subjects, were included in the mainstream population and were defined as “FET-worried patients.”

The third category had the lowest score of all 19 measurement statements and was concluded to be the “unknown” state of FET. They presented a fuzzy cognitive state in the interview, were defined as “FET-fuzzy patients,” and accounted for 9.8% of the total patients.

3.3.2. Attitude changes in the 3 groups of patients after clinical data presentation. After finishing the 19 attitude statements, patients were shown a related Nordic cohort study, in which relative data was highlighted. Twelve other measurement statements were presented for scoring to observe whether the clinical data had an effect on the attitudes of patients.

Table 2 shows that for FET-not-needed patients, even if clinical data was shown, these patients did not change their attitude

Table 2
Attitude statements and grouping based on patient attitudes.

Attitude statements	FET-worried patients (72.7%)	FET-fuzzy patients (9.8%)	FET-not-needed patients (17.5%)
	Average	Average	Average
I do not understand FET and need to the doctor’s advice	3.18	4.14	2.86
I do not know the current freezing techniques, and I’m worrying embryos freeze to death	2.30	2.78	1.05
I feel the success rate of FET is almost the same as ET	2.50	2.75	0.22
I think it is necessary to minimize such vitro manipulation like whole embryo freezing, in order to reduce damage to the embryo. If I can receive ET, I will not try FET	2.33	2.96	0.81
I need to know how long FET has been used in clinic, and how save it is	2.05	4.44	2.78
I want to know how many centers in or out of China are popularizing FET	1.68	4.25	2.22
I need clinical statistic data to estimate the difference of success rate between FET and ET	2.71	4.42	2.65
I am concerned how much FET could reduce the risk of maternal complications	2.79	4.18	2.03
I am concerned how much FET would reduce the morbidity of the baby, and even the next generation of the baby	3.06	4.27	2.08
When ovulation, the drugs used will make hormone levels rise, a lot of factors in mother’s body will change, these changes may affect the safety of motherhood and baby	3.3	3.66	0.51
When receiving FET, there would be a 3-month break before transplantation. During this time, I could regulate the body, do some physical exercise, the uterine environment and maternal health could be a little better.	2.73	3.63	0.68
It is unknown how much FET would reduce the morbidity of the baby, and even the next generation of the baby, I would take FET with a grain of salt	3.58	3.89	1.19
I wanted to get pregnant as soon as possible, no matter what technology I would take	3.48	3.62	0.73
FET needs 3 months to wait, I cannot afford the time costs	3.20	3.08	2.00
FET needs 3 months to wait, but I am much anxious, and do not want wait	3.44	3.59	2.24
With the age growing older, the pressure from family and friends would be much heavier, so I want to get pregnant quickly	4.06	4.16	2.78
I live far from the hospital, FET would increase the commute, accommodation, and other related costs	3.47	3.37	1.95
Perhaps these 2 methods are similar, the hospital just mobilize us in order to increase the economic benefits	2.23	2.45	1.05

ET = embryo transfer, FET = frozen-thawed embryo transfer.

toward FET, which were affected by their socioeconomic factors. For the largest proportion of FET-worried patients, the effect of persuading was most obvious, in which attitude statements such as “hope that the hospital show similar data,” “hope to see larger sample size data,” and “would like to see domestic clinical data” had mean points above 4 (agree to totally agree). The smallest proportion of FET-fuzzy patients continued to show on the statement of “fuzzy cognitive” state, with mean points of ~3 (neutral), indicating that even if relevant data was shown, this patient population would continue to remain in the “cognitive chaos” state.

3.3.3. Portrait analysis of the 3 groups of patients. (1) “FET-not-needed patients” (17.5%): relatively young, low income, residing outside of Beijing. Patients in this category were the youngest and almost from the low line region (Hebei and Inner Mongolia), and their household income levels are relatively low (average monthly household income was < 8000 yuan; accounted for 74.2%, which was much higher than the other 2 groups [45.9% and 44.9%, respectively]). These situations show a reasonable explanation why these patients held a basic negative attitude toward FET, which was affected by socioeconomic factors (time costs, energy costs, or expenses costs). For the Center for Reproductive Medicine, the People’s Hospital of Peking University, the likelihood for these patients to undergo FET was lowest, and the cost of education was relatively higher.

(2) “FET-worried patients” (72.7%): middle-aged people, no children. Most of these patients were 45 to 54 years old. Approximately 95.6% of these patients had no children, which was higher than the other 2 categories (87.9% and 91.9%, respectively). A relatively larger number of patients in this category had experienced a failed test-tube baby surgery (23.4% vs 16.7%, and 21.6% in the other 2 categories).

“Middle-aged people, no children, had experienced failure tubes,” led to a comprehensive second class of patients both on the “whole embryo freezing” technique rational concerns, and there was some loss and anxiety, in which only few could indicate as the “rational acceptance” of the comparative advantage of the

technology. These patients are a sample of patients in the mainstream population, are the most vulnerable to reproductive centers, doctor’s guidance and education; accept for the “whole embryo freezing” technology groups.

(3) “FET-fuzzy patients” (9.8%): no experience, no knowledge. Patients who never heard of FET were the highest relative proportion (67.6% vs 30.3%, and 38.7% in the other 2 categories). These patients were in the “cognitive chaos” state, and needs more clear and professional guidance and information from hospitals and doctors.

3.4. Requirement of FET technology information in patients

Nearly 82.5% of patient samples approve “the expertise from the hospitals and doctors,” and ~54.1% of these patient samples approve “clinical data.”

For the mode of transmission, the hospital official website is the most trusted of the top 5 information channels, followed by doctors’ individual social media accounts, third-party inquiry platform, telemedicine platform, and patients’ social media groups.

For the literacy of FET, a set of open-ended questions were also conducted to ask for relevant recommendations from the patient. The “voice of the patients” for “clinical cases” and “explanations in detail from physicians” was the most intense in the 90 patients who gave advices (the remaining samples did not show any recommendation, Table 3). Some certain advices were remarkable: “Hospitals should loop play the science knowledge video,” “It is necessary to promote if FET is good, and specific costs and time cycle should be clear,” “The information should be widely spread, but the doctors were too busy to spread this information,” “How to fully use the 3-month waiting period to prepare for the transplant should be introduced,” “How to reduce the failure rate of thawed embryos should be explained to increase patients’ confidence,” “There is not enough propaganda, it’s better to build a test tube app or something,” “The popularity is not high, so the patients can only listen to the doctors’

Table 3

Attitude statements of 3 groups patients after clinical data presenting.

Attitude statements	FET-worried patients (72.7%)	FET-fuzzy patients (9.8%)	FET-not-needed patients (17.5%)
	Average	Average	Average
These data well, so I understand FET could significantly decrease the complications	3.85	3.19	3.65
I hope the hospital can clearly demonstrate these data to the patient, in order to show the advantages of FET	4.14	3.59	3.97
I would like to see a larger sample of data to prove the advantages of FET	4.19	3.51	3.77
These data do not demonstrate that FET could significantly reduce maternal complications as I imaged	3.65	3.00	3.38
These data do not demonstrate that FET is much safer as I imaged	3.63	3.03	3.48
Although these research data can explain some problems, but I still want to see more clinical data in China	4.15	3.51	3.64
Although the data prove that FET can more effectively reduce maternal complications, but I still tend to choose ET	3.33	2.68	3.15
I do not care the data of FET, I just want to get pregnant quickly	3.36	2.86	3.47
I cannot select the FET, because I cannot afford the time and effort costs	2.84	2.41	3.00
Data are no sense to me, I do not understand, I need doctors’ recommendations	3.85	3.3	3.88
Data are no sense to me, I do not understand, I believe the real experiences and recommendations from patients around	3.35	2.73	3.58
In China currently only the Shanghai 9th hospital implemented FET, I hope such hospitals could be more	3.46	2.92	3.14

ET = embryo transfer, FET = frozen-thawed embryo transfer.

Table 4
Advices of patients about propagandizing FET (open questionnaire).

Advices	Frequency
More clinical cases to show	15
More detailed explanation from the doctors	11
Popularization	7
Videos to play hospital or related popularity	6
Lectures	6
Using the media, strengthen the propaganda	5
Better understanding	4
To provide more data/global statistics	4
Patient communication (social media/face to face)	4
We would like to see the technology is mature	3
TV	3
Official channels for popularity	3
Books/brochures	3
More straightforward approach to universal	2
If good, the need to promote, clarify the costs and cycle	2
Website/APP	2
Hope the hospital could do better	1
Professional reading	1

FET = frozen-thawed embryo transfer.

recommendations, and there is a lack of choices,” “Hospitals should establish a corresponding consulting room,” and “Hospitals should establish a propaganda department” (Table 4).

4. Discussion

ART technology has been widely used in the world. With the development of technology, the number of patients who under-

went FET also gradually increased. Pregnancy rate and live birth rate of FET have been close to or above ET.^[7,8] It is considered that by avoiding the influence of controlled ovarian stimulation (COS) on the uterus, endometrium, and embryo, FET can effectively reduce the incidence of pregnancy complications, premature birth, early yield, low birth weight children, small for gestational age children, huge children, and neonatal death.^[9-14,16]

Evans et al^[17] considered that although the evidence of the advantage of FET gradually improves, the awareness of patients and government policies continues to have a large extent of influence on the selection of the ART method. Hope and Rombauts^[18] Martini et al,^[19] as well as Stillman et al^[20] had already investigated the attitude of patients on FET and single embryo transfer in their countries, but there is no such study in China.

We first took small lectures to collect questions and views, in order to understand the current awareness and expectations of IVF procedure-related patients on FET. This was followed by another large-scale investigation, in order to learn about the attitude to FET of patients in Beijing, who were aged 25 to 44 years and had an intermediate socio-economic level. Clustering results based on quantitative measurement revealed that these mainstream groups of patients were “FET-worried patients.” They are “middle-aged, childless, and had a tube failure experience.” They not only have rational concerns on the FET technique, but also some loss and anxiety. Few of them may accept the comparative advantages of the technology. Meanwhile, this group was much vulnerable to reproductive centers, doctors’ guidance and education, and accepted the FET technology in the end. Other types of patient populations were “FET-not-needed patients” and “FET-fuzzy patients.” The former was mainly affected by socio-economic characteristics and presented a rigid demand to FET technology. Even though clinical data was shown, their attitudes were hard to change. The latter was the lowest proportion in the population, and was

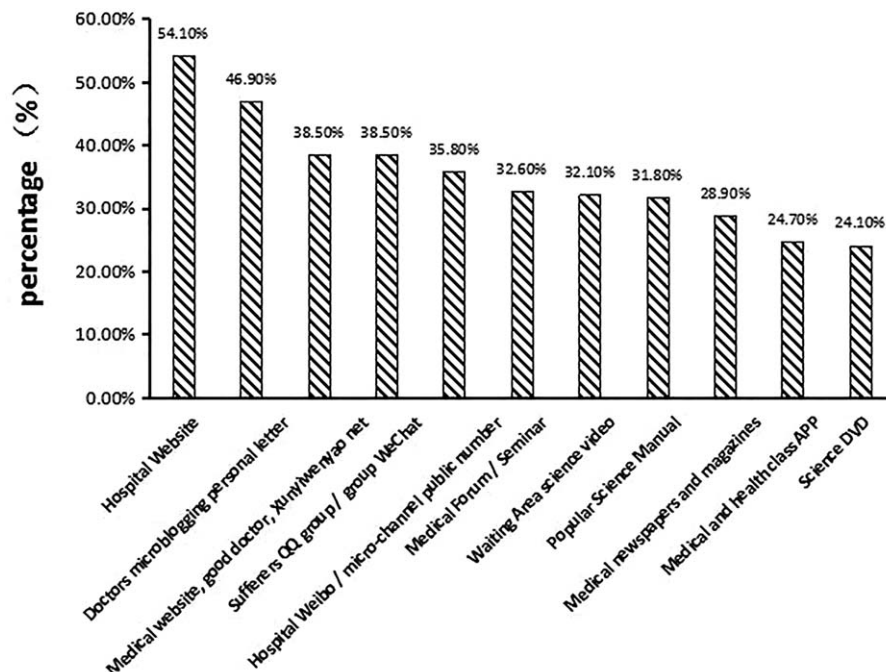


Figure 1. Preferences of propagation mode about FET in patients. FET = frozen-thawed embryo transfer.

mainly affected by individual surgical experience. In the state of “no experience, knowledge gaps,” and even though relevant data was shown, such patient population remained in the “cognitive chaos” state. These patients need hospitals and doctors to provide more clear information and professional guidance.

From patients’ attitudes, official advice, guidance, and instructions from doctors were recognized by patients, but clinical data and cases are also convincing means. The study of Hope et al^[18] demonstrated that the influence of video clips (DVD) on a patient’s ART method selection was greater than that of a brochure. By contrast, Chinese patients preferred more professional and improved data from hospitals and doctors (54.1% vs 24.1%, Fig. 1), which might be biased by the higher education level of patients in our sample (Junior college degree or above 75.3%). Propaganda needs of patients focused on 11 kinds of ways (Fig. 1), in which a higher proportion of opinions such as “hospital site,” “Doctor’s personal blog, we-chat” and other comments were easy to implement as medical institutions and individual doctors. Wider publicity might require hospitals to cooperate with related companies. From the immediate needs of patients, more information and data on clinical outcomes and complications of FET was more required. However, there is a lack of such studies in China at present, and only a few small-scale data are available. There should be more large-scale and multicenter clinical studies to provide reference for Chinese patients.

There is a strict family planning policy in China. Patients with children do not attempt to have more children through ART. Thus, the basis of this study population may have a significant difference with other countries. The national health care system is another important condition for the attitudes of patients to FET. Different with health insurance in other countries, ART-related health care costs will be borne entirely by the patients themselves, in China. This restricts the development of ART in China, in which many economically disadvantaged families cannot receive timely diagnosis and treatment.

In January 2016, China introduced a new family planning policy, which is the permission to have a second child. Hence, older patients would carry out assisted reproduction. This way, there would be bias in our follow-up study groups. Therefore, a larger and lengthier investigation is needed. This study covers the main areas in Beijing, Hebei, Inner Mongolia, and other places. Participants in this study were 20 to 35 years old, childless, and were in the middle socio-economic level patient population. However, this is only a single-center study, and more extensive research is needed.

Patients were limited to the rigid demand, economic level, education, and awareness. The acceptance of FET is different, and the degree of acceptance on change after publicity is also different. Patients are more receptive to the hospital and doctor’s advice and guidance. Therefore, we need to conduct large-scale and multicenter clinical studies to provide a reference for Chinese patients.

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