Nanjing consensus on methodology of washed microbiota transplantation

Fecal Microbiota Transplantation-standardization Study Group

The methods of fecal microbiota transplantation (FMT) and the related results vary a lot among centers worldwide. Therefore, methodologic standardization can improve the clinical practice and trials about FMT. A panel of 28 experts from 22 hospitals or institutes in 15 cities has contributed to the present consensus on washed microbiota transplantation (WMT).[1] This consensus provides guidance on the methodology of WMT, which is different from that of the manually FMT in recent experts' consensus or recommendations.[2,3] All experts were assigned, according to their expertise, to the following five groups: Group 1, donor screening; Group 2, washing microbiota protocol, storing, and transport; Group 3, patient preparation; Group 4, delivery decision; Group 5, safety and management. Each statement and the following comment have passed a Delphi process and a face-to-face plenary meeting. The best available evidence was assessed according to the Grading of Recommendations Assessment, Development and Evaluation system.

Consensus was reached for all 31 statements after three rounds of anonymous voting and editing. Respectively, 100% of statements passed the 80% agreement threshold after the first round, 100% after the second round, and 100% after the third round. In the final round, all statements were presented to 28 of 28 (100%) panel members on December 12, 2019 in Nanjing, China, for a face-to-face meeting. The consensus report is shown in Table 1.

The methods of the consensus development process, each statement and the related quality of evidence, strength of recommendation/expert opinions, and comments with evidence are shown in Supplementary File 1, http://links.lww.com/CM9/A255. The brief laboratory methods for the preparation of washed microbiota suspensions are shown in Table 2.

Contributors: Fa-Ming Zhang conceived, organized, and developed the project. Siew Chien Ng, Xing-Xiang He, Deng-Chyang Wu, Kai-Chun Wu, and Cheng-Tang Chiu chaired the working group 1, group 2, group 3, group 4, and group 5, respectively. All panel members joined the consensus development and manuscript revision, and approved the final manuscript.

Experts of FMT-standardization Study Group: Qing Cao, Shanghai Children's Medical Center; Paul Kay Sheung Chan, Chinese University of Hong Kong; Cheng-Hsun Chiu, Chang Gung Memorial Hospital; Cheng-Tang Chiu, Chang Gung Memorial Hospital; Bo-Ta Cui, Second Affiliated Hospital of Nanjing Medical University; Ming-Ming Deng, Affiliated Hospital of Southwest Medical University; Ying Fang, Children's Hospital of Xi'an City; Bai-Sui Feng, Second Affiliated Hospital of Zhengzhou University; Xing-Xiang He, First Affiliated Hospital of Guangdong Pharmaceutical University; Wen-Hung Hsu, Kaohsiung Medical University Hospital; Yun-Lian Hu, Hubei Hospital of Traditional Chinese Medicine; Jing-Nan Li, Peking Union Medical College Hospital; Yi Li, Sir Run Run Hospital of Nanjing Medical University; Yu Liu, Sir Run Run Hospital of Nanjing Medical University; Ying-Lei Miao, First Affiliated Hospital of Kunming Medical University; Siew Chien Ng, Chinese University of Hong Kong; Yong-Zhan Nie, Xijing Hospital of Digestive Diseases; Jun Wang, Chinese Academy of Sciences; Jun-Ping Wang, Shanxi Provincial People's Hospital; Deng-Chyang Wu, Kaohsiung Medical University; Kai-Chun Wu, Xijing Hospital of Digestive Diseases; Fang Xiao, Tongji Hospital; Shao-Qi Yang, General Hospital of Ningxia Medical University; Yong Yu, Fifth Affiliated Hospital of Zhengzhou University; Fa-Ming Zhang, Second Affiliated Hospital of Nanjing Medical University; Xiao-Yin Zhang, Third People's Hospital of Shenzhen; Yong-Jian Zhou, Guangzhou First People's Hospital; Yin Zhu, First Affiliated Hospital of Nanchang University.

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Correspondence to: Prof. Fa-Ming Zhang, Medical Center for Digestive Diseases, the Second Affiliated Hospital of Nanjing Medical University, 121 Jiangjiayuan, Nanjing, Jiangsu 210011, China
E-Mail: fzhang@njmu.edu.cn

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Table 1: Statements released by Nanjing consensus on the methodology of washed microbiota transplantation.

Statements	QoE	SoR
Part 1: Donor screening		
1. Education targeting candidate donors for FMT should be taken to increase their willingness to donate feces	Low	Strong
2. Candidate donors must be informed of the potential risks and benefits of FMT for recipients	Low	Strong
3. A questionnaire interview has to be conducted to exclude candidates with risk factors in their medical history and lifestyle habits at the beginning of the screening	Moderate	Strong
4. Donors who have passed the primary screening have to undergo a face-to-face interview with a trained physician	Low	Strong
5. Potential donors who have passed the secondary screening have to undergo blood and stool testing to rule out transmissible infectious diseases and potential dysbiosis-related disease. The laboratory screening should be scheduled within three weeks before donation	Moderate	Strong
6. Donors with repeat donations should undergo monitoring screening: (a) scheduled screening; (b) after holiday or travel; (c) recovery from sickness or other potential conditions in which physicians think the donors need to be retested	Low	Strong
7. Eligible donors have to undergo a questionnaire on the day of donation to exclude any interim risk factors	Moderate	Strong
8. Donors are instructed to report any blood, mucus, or change in stool consistency noticed in the donated stool	EO	EO
Part 2: Washing microbiota protocol, storage, and transport		
9. Washed microbiota preparation contributes to reduced FMT-related AEs	Low	Strong
10. Quality control of washed microbiota preparation is pivotal for improving the acceptance of FMT from patients and physicians	Low	Strong
11. Limiting the time from stool collection to microbiota delivery is conducive to preserving functional fecal microbiota	Low	Strong
12. Quality control of washed microbiota preparation is dependent on appropriately qualified facilities	Moderate	Strong
13. Washed microbiota can be stored at −80°C for up to 1 year by adding glycerol, a cryoprotective agent, to a final concentration of 10%. Frozen microbiota should be thawed in a warm (37°C) water bath before using it	Moderate	Strong
14. Frozen washed microbiota materials should be sealed and remained frozen during transportation	EO	EO
15. Frozen washed microbiota suspensions can be stored with dry ice or in a freezer at <−20°C for temporary storage or transportation	EO	EO
Part 3: Patient preparation		
16. Patients or their guardians should be informed of the donor source and the methods of microbiota preparation	EO	EO
17. Antibiotics should be stopped 12–48 h before microbiota delivery	Low	Strong
18. The decision on bowel lavage before microbiota delivery should be considered based on patients' conditions	Low	Weak
19. All recipients of WMT should undergo blood testing for transmissible infections	EO	EO
Part 4: Delivery decision		
20. Aspiration pneumonia is a serious AE that can be related to FMT delivery methods	Moderate	Strong
21. Washed microbiota can be delivered into mid-gut through the endoscopic channel, nasojejunal tube, gastrostomy tube, or jejunostomy tube	Moderate	Strong
22. Washed microbiota suspensions can be delivered through colonic TET	Low	Strong
23. Colonic infusion under colonoscopy can be considered when a single infusion is sufficient for the patient	High	Strong
24. Microbiota delivered by enema might be less effective than colonoscopy and colonic TET	Low	Strong
25. Conscious patients with CDI who can tolerate capsules are suitable to choose capsulized preparation of washed microbiota	High	Strong
26. Suitable conscious pediatric patients who have no other alternative can be given washed fecal microbiota suspensions through the nasogastric tube	Moderate	Strong

(*continued*)

Table 1
(continued).

Statements	QoE	SoR
Part 5: Safety and management		
27. The clinical governance of WMT is mandatory. The service should be provided by trained physicians	EO	EO
28. The stool sample from a donor should be stored for at least 2 years for safety traceability. The donor screening documentation and laboratory records should be stored for at least 10 years	Low	Strong
29. Regional WMT center in the hospital is encouraged to provide professional WMT services and microbiota-related researches	Low	Strong
30. The laboratory condition for WMT is required to meet level 2, and encouraged to meet level 3	EO	EO
31. The staff of the WMT center must receive training on WMT	EO	EO

AE: Adverse event; CDI: *Clostridium difficile* infection; EO: Expert opinions; FMT: Fecal microbiota transplantation; QoE: Quality of evidence; SoR: Strength of recommendation; TET: Trans-endoscopic tubing; WMT: Washed microbiota transplantation.

Table 2: General steps for the preparation of washed microbiota suspensions.

1) Feces should preferably be collected on-site in a disposable feces container in a dedicated room only for donors
2) All devices directly contacting fecal matters used for the fecal collection, suspension filtration, centrifugation, and washing should be disposable
3) Feces from adults less than 50 g are not recommended proceeding in the process using an automatic purification system for enriching microbiota
4) The fecal suspension is transferred to centrifugation tubes for centrifugation with 700 × *g* for 3 min and discard the supernatant
5) This is repeated three times using sterile saline to make the suspension
6) 10 cm^3 (about 1.0×10^{13} bacteria) of final precipitated microbiota is the basic unit dose for clinical use. The volume ratio of final precipitation/vector solution is 1:2 for making suspensions as fresh or frozen use
7) Anaerobic fecal processing is encouraged if possible

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Conflicts of interest

Fa-Ming Zhang conceived the concept of GenFMTer and transendoscopic enteral tubing and devices related to them. The other authors declare no conflict of interest.

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