

Cooperative Adenomyosis Network (CAN)

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A. OBJECT

5000 women diagnosed of Adenomyosis(AM) with pathology or magnetic resonance image (MRI) will be enrolled from nationwide multicenter. Each center should recruit at least 200 patients.

— **PATHOLOGY** :Adenomyosis can be present diffusely throughout the myometrium, or confined to a discrete area. Upon sectioning the uterus, the myometrial wall appears thickened and often contains small hemorrhagic or chocolate colored areas representing islands of endometrial bleeding. The term cystic is used to describe either diffuse adenomyosis or adenomyomas for which with cysts >5 mm in diameter.

-TRANSVAGINAL SONOGRAPHY:

1. Uterine enlargement—Globular uterine enlargement that is generally up to 12 cm in uterine length and that is not explained by the presence of leiomyomata is a characteristic finding.
2. Cystic anechoic spaces or lakes in the myometrium—The cystic anechoic spaces within the myometrium are variable in size and can occur throughout the myometrium. The cystic changes in the outer myometrium may on occasion represent small arcuate veins rather than adenomyomas. The application of color Doppler imaging at low velocity scales may help in this differentiation.
3. Uterine wall thickening—The uterine wall thickening can show anteroposterior asymmetry, especially when the disease is focal.
4. Subendometrial echogenic linear striations—Invasion of the endometrial glands into the subendometrial tissue induces a hyperplastic reaction, which appears as echogenic linear striations fanning out from the endometrial layer.
5. Heterogeneous echo texture—There is a lack of homogeneity within the myometrium with evidence of architectural disturbance. This finding has been shown to be the most predictive of adenomyosis.
6. Obscure endometrial/myometrial border—Invasion of the myometrium by the glands also obscures the normally distinct endometrial/myometrial border.
7. Thickening of the transition zone—This zone is a layer that appears as a hypoechoic halo surrounding the endometrial layer. A thickness of 12 mm or greater has been shown to be associated with adenomyosis.

—**PELVIC MRI:**

1. Thickening of the junctional zone(JZ) ≥ 12 mm
2. Greatest JZ thickness to total myometrium ratio $> 40\text{--}50\%$ (connected to muscular hypertrophy).
3. Foci of high signal intensity running alongside the endometrium on T2 and sometimes also T1-weighted images that persist on Fat-Sat (FS)

B. STUDY DESIGN AND METHOD

—**STUDY DESIGN:** A Prospective Multicenter Observational Cohort Study

—**METHODS:**

Period: 3 years, including 6 months for building up Network platform and database, 30 months for the follow-up with an interval of at least once every 6 months done for every patient and updating the database timely.

C. TECHNICAL ROUTE

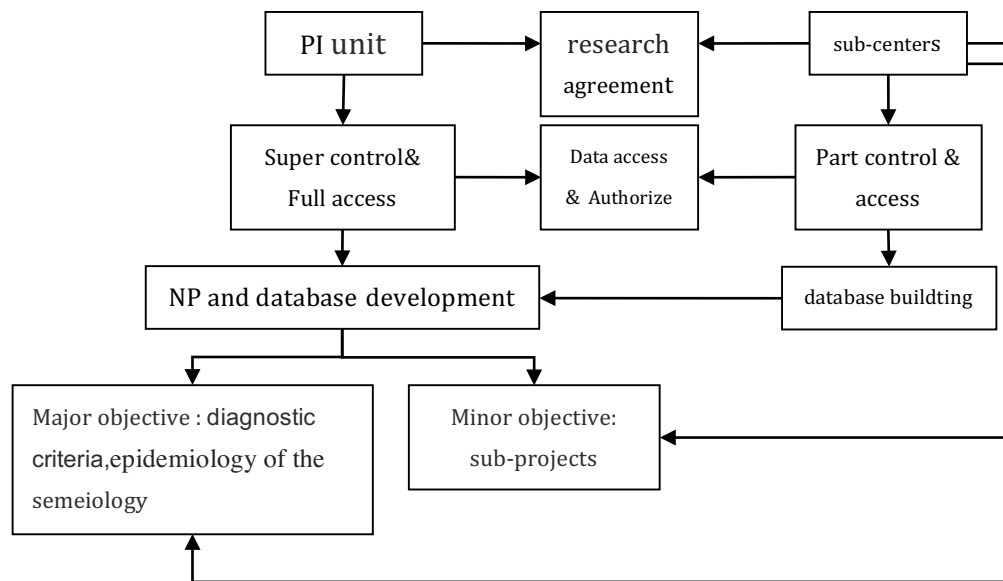
1. **Build up database basing on the Network platform.** Licensed research centers recruit patients according to the consistent universal diagnostic criteria, and then extract and register clinical pathologic data from their medical records system after getting their informed consent. Limited sharing platform for the database entry would be built by expert network firms, making it available for sub-centers to access the database and download relevant data. Ultimately, on the premise of research results sharing, we could carry out clinical scientific research development and summary nationwide.

[Picture 1.]

Clinical pathologic data:

- 1). Characteristics of epidemiology (Age, reproductive history, menstrual history, body parameters)
- 2). Diagnostic criteria (pathology, transvaginal ultrasonography or magnetic resonance image)
- 3) Semeiology and evaluative criteria (vision algetic standard (VAS) ; pictorial blood loss assessment chart (PBAC))
- 4) Surgical approach and perioperative reproductive techniques program
- 5) Medical treatment
- 6) Reproductive choices and fertility outcomes
- 7) Symptom improvement, quality and satisfaction of Life
- 8) Malignant transformation
- 9) Menopausal symptoms and Hormone therapy
- 10) Systematic assessment of the side effects

Picture1. Network platform(NP) and database Building



2. Based on the database informations, 30-month follow-up will be done for every patient, trying to analyze the problems below : 1) The diagnostic strategies for AM;2) Selection of therapeutic scheme;3) Etiology of AM and endometriosis;4)The study of histology、 molecular and genetics about AM and endometrial receptivity.
3. The Follow-up visits is standardized, and the contents include :1) The therapeutic efficacy, complication and side-effect of different treatments;2)The fertility outcomes of different reproductive choices;3) AM &menopausal symptoms and hormone therapy ; 4) Relevant issues among malignant transformation of AM.
4. According to the data above, intensive training courses about AM will be organized regularly, finally propeling the formation of Expert Consensus and Clinical Guidelines about AM which suitable to chinese conditions.

D. STATISTICS ANALYSIS

Categorical data is analyzed by Chi-square test, and continuous data is analyzed by T test. If the baseline characteristics are similar, the chi-square test can be used directly to compare the incidence rates between the group of exposure and the group of non-exposure, to conclude if there is a correlation between the exposure factor and outcome. In a meanwhile, calculate the relative risk and 95% confidence interval in order to further illustrate the degree of correlation. In contrast, if the baseline characteristics of exposure group and non-exposure group are different, multiple factor linear regression should be used to control the

mixing factors. If there is no time variation in the data, logistic linear regression can be used to adjust the baseline characteristics of the groups which are different in the model. If there are time variations in the data, Cox linear regression should be used to adjust the baseline characteristics of the groups which are different in the model.

E. QUALITY CONTROL MEASUREMENT AND RESULT PUBLICATION

1. Every center of the research possesses the competence of scientific research to conduct clinical studies. Special people from each center will be put in charge of the research and monitoring the whole procedure. The rights and interests, responsibility and obligation of all centers will be standardized with the research agreement.
2. The maintenance, secrecy and safety of Network platform and database will be guaranteed by Department of Obstetrics and Gynecology, Peking Union Medical College Hospital.
3. Every center is responsible for the database building, and required to finish the prospective follow up for 200 patients at least.
4. The researchers' findings will be released in a paper published online.

F. SOURCE(S) OF FUNDING

1. This study does not charge any fee to any patients.
2. The major cost of the study, a total of 300000 RMB, comes from the special financial funds set up by Chinese Medical Doctor Association Division of Gynecologic Endocrinology and Chinese Maternal and Child Health Association Division of Gynecologic Endocrinology.