Does the combination of hysterectomy and general anesthesia increase the risk of subsequent development of dementia?

Wen-Ling Lee[a,b,c], Li-Te Lin[c,d,e], Peng-Hui Wang[c,f,g,h,*]

[a]Department of Medicine, Cheng-Hsin General Hospital, Taipei, Taiwan, ROC; [b]Department of Nursing, Oriental Institute of Technology, New Taipei City, Taiwan, ROC; [c]Institute of Clinical Medicine, National Yang-Ming University, Taipei, Taiwan, ROC; [d]Department of Obstetrics and Gynecology, Kaohsiung Veterans General Hospital, Kaohsiung, Taiwan, ROC; [e]Department of Biological Science, National Sun Yat-Sen University, Kaohsiung, Taiwan, ROC; [f]Department of Obstetrics and Gynecology, Taipei Veterans General Hospital, Taipei, Taiwan, ROC; [g]Department of Medical Research, China Medical University Hospital, Taichung, Taiwan, ROC; [h]Female Cancer Foundation, Taipei, Taiwan, ROC

Total hysterectomy (TH) may be one of the most frequent surgeries in women during their life-span period, although the recent trends have become more apparent in the use of fertility-sparing surgery (organ-preservation strategy) in place of the original removal of the entire organ (uterus),[1–4] since the uterus has been regarded as the regulator and controller of important physiological functions, a sexual organ, a source of energy and vitality, and a maintainer of youth and attractiveness.[5] Therefore, long-term TH-related morbidity or health issue is worthy of our attention. We are happy to learn one article addressing this topic published in the April issue of the *Journal of the Chinese Medical Association*.[6] The authors conducted a retrospective cohort study to evaluate the risk of dementia in women who had been treated with TH using the 14-year National Health Insurance Database (between 2000 and 2013).[6] The authors found that age at surgery and anesthesia method were strongly associated with the subsequent development of dementia in women having treated with TH.[6] The results showed that the hazard ratio (HR) for general anesthesia (GA) to develop dementia was a 2.68-fold increase (95% confidence interval [CI] 1.27-5.65) compared with that for regional anesthesia (RA).[6] In addition, the risk of dementia increased by 7.4% for every 1-year increase in age (HR 1.07, 95% CI 1.05-1.10).[6] It is much interesting to find the relationship between the development of dementia and age (≤50 or >50 years of age (younger population vs older population) in Dr. Chen's study, since the authors found that the risk of dementia increased by 13% for every 1-year increase in age (HR 1.13, 95% CI 1.13-1.13), suggesting that the risk of developing dementia in women treated with TH was more apparent in the older population receiving GA.[6] By contrast, HR of the developing dementia in the older population treated with GA was only 1.21 (95% CI 1.06-1.38), which was significantly lower than the 2.68-fold increase of dementia in the whole population, regardless of younger age or older age.[6] The conflicted data presentation is worthy of further discussion.

First, it is still uncertain in the Chen's study to enroll how many subjects for analysis, since the study population seemed to be different between the abstract section and the main text. The former was 280 308 patients but the latter was 276 913. Therefore, it is unclear on the real incidence of dementia in women who has been treated with TH.

Second, it is well known that there are many surgical methods available to perform the TH in the clinical practice, including minimally invasive surgery, natural orifice surgery, and/or conventional exploratory laparotomy.[7–9] All operative procedures need anesthesia, regardless of the use of RA (including spinal anesthesia, epidural anesthesia, and/or local anesthesia) or GA. However, there is no doubt that GA is most frequently applied for TH, regardless of which approach, such as total abdominal hysterectomy, total vaginal hysterectomy, or laparoscopically assisted vaginal hysterectomy was used. In fact, the authors also showed that 93.63% (n = 259 270) of patients received GA for their TH.[6] If the GA is really strongly associated with the subsequent development of dementia in women, especially in younger women (age <45 years shown by authors)[6] who need TH, what should we do for these women? Do we highly recommend that these patients had better undergo RA or other non-GA method if they should receive TH surgery as the risk of dementia is increased in women treated with the combination of TH and GA? Therefore, the absence of any one of the aforementioned procedures (either TH or GA) may ameliorate the risk of the developing dementia. That makes us question why we should perform TH for benign lesion. Since the current trend has favored the fertility-sparing surgery (organ-preservation strategy) in all women with benign uterine lesions, even for those older women, who might be informed that this consideration (fertility preservation) is never needed, do we suggest that these women should be treated with fertility-preservation uterine surgery in place of TH? It is unclear that the increased risk of dementia after GA procedure could be reproducible in the women who undergo fertility-preservation uterine surgery.

*Address correspondence. Dr. Peng-Hui Wang, Department of Obstetrics and Gynecology, Taipei Veterans General Hospital, 201, Section 2, Shi-Pai Road, Taipei 112, Taiwan, ROC. E-mail addresses: phwang@vghtpe.gov.tw; or pongpongwang@gmail.com (P.-H. Wang).

Conflicts of interest: The authors declare that they have no conflicts of interest related to the subject matter or materials discussed in this article.

Journal of Chinese Medical Association. (2021) 84: 1-2.

Received September 10, 2020; accepted September 10, 2020.

doi: 10.1097/JCMA.0000000000000436.

The other question is that TH might not be always avoided. For example, obstetric emergency is the best example. Peripartum TH is a rescue method for saving life in the management of women with uncontrolled severe maternal hemorrhage if all conservative treatments are in vain.[10] For those critical patients, it is nearly impossible to use RA in place of GA to perform the urgent peripartum TH. As shown by Dr. Chen's study, combination of TH and GA in the women younger than 50 years has a higher risk of further development of dementia,[6] contributing to a biggest challenge for clinicians to face this dilemma. If the finding was true in Dr. Chen's study, the results might increase much unnecessary anxiety for those women. We believe that these pregnant women never image that they may lose their fertility ability in total. If they are informed or not informed that they may have an additional risk to develop dementia after TH and GA, this catastrophic nightmare may make them more suffering. Therefore, this interpretation might significantly influence our routine practice. In a recent publication by Dr. Kang, the results also had the similar challenge,[11] since some findings from the study might be co-incidental and the clinical significance may be low.[12] In this dilemma, the underlying cause to induce anxiety or suffering of patients cannot be easily overcome, even though we have tried our best to convince the patients.[12] We are worried about the data presentation, since the results might not further improve the care of the patients.

With far-advanced development of medication, conservative treatment in place of the original invasive procedure, such as surgery, is predictable. We believed if maximal reduction of the need for surgery can be reached, all surgery-related morbidity or mortality could be expected to be decreased dramatically. No surgery means no surgery-related morbidity or mortality. No TH is performed, contributing to no need of GA. As expected, the risk of dementia will not be increased.

Finally, the research papers may provide us much information; however, we believe that any information should be useful or practicable in the clinical practice. At least, the absolute risk and benefit ratio should be well informed when any conclusion is made.

ACKNOWLEDGMENTS

This article was supported by grants from the Ministry of Science and Technology, Executive Yuan, Taiwan (MOST 109-2314-B-075B-014-MY2 and MOST 109-2314-B-075-056), and Taipei Veterans General Hospital (V109C-108, and VGH109E-005-5). The authors appreciate the support from Female Cancer Foundation, Taipei, Taiwan.

REFERENCES

1. Chang CP, Hsu FK, Lai MJ, Chang WH, Lee NR, Lee HL, et al. Uterine-preserving pelvic organ prolapse surgery using the UPHOLD LITE vaginal support system: the outcomes of 291 patients. *Medicine (Baltimore)* 2019;**98**:e15086.
2. Tsai CP, Kao HF, Liu CK, Shen PS, Chen MJ, Hung MJ. One-year outcomes of a suture-less laparoscopic sacral hysteropexy using polypropylene Y-mesh grafts and fibrin sealant spray: a prospective comparative study. *J Chin Med Assoc* 2020;**83**:484–90.
3. Li YL, Chang YW, Yang TH, Wu LY, Chuang FC, Kung FT, et al. Mesh-related complications in single-incision transvaginal mesh (TVM) and laparoscopic abdominal sacrocolpopexy (LASC). *Taiwan J Obstet Gynecol* 2020;**59**:43–50.
4. Chiu CS, Hwu YM, Lee RK, Lin MH. Intrauterine adhesion prevention with Malecot catheter after hysteroscopic myomectomy: a novel approach. *Taiwan J Obstet Gynecol* 2020;**59**:56–60.
5. Huang CY, Chang WH, Cheng M, Huang HY, Horng HC, Chen YJ, et al. Crosslinked hyaluronic acid gels for the prevention of intrauterine adhesions after a hysteroscopic myomectomy in women with submucosal myomas: a prospective, randomized, controlled trial. *Life* 2020;**10**:67.
6. Chen YC, Oyang YJ, Lin TY, Sun WZ. Risk assessment of dementia after hysterectomy: analysis of 14-year data from the National Health Insurance Research Database in Taiwan. *J Chin Med Assoc* 2020;**83**:394–9.
7. Lee YL, Hsu TF, Jiang LY, Chao HT, Wang PH, Chen YJ. Transvaginal natural orifice transluminal endoscopic surgery for female-to-male transgender men. *J Minim Invasive Gynecol* 2019;**26**:135–42.
8. Sao CH, Chan-Tiopianco M, Chung KC, Chen YJ, Horng HC, Lee WL, et al. Pain after laparoscopic surgery: focus on shoulder-tip pain after gynecological laparoscopic surgery. *J Chin Med Assoc* 2019;**82**:819–26.
9. Deura I, Shimada M, Azuma Y, Komatsu H, Nagira K, Sawada M, et al. Comparison of laparoscopic surgery and conventional laparotomy for surgical staging of patients with presumed low-risk endometrial cancer: the current state of Japan. *Taiwan J Obstet Gynecol* 2019;**58**:99–104.
10. Bilgin Z, Kömürcü N. Comparison of the effects and side effects of misoprostol and oxytocin in the postpartum period: a systematic review. *Taiwan J Obstet Gynecol* 2019;**58**:748–56.
11. Kang CM. Effects of psychological intervention and relevant influence factors on pregnant women undergoing interventional prenatal diagnosis. *J Chin Med Assoc* 2020;**83**:202–5.
12. Sun HD, Yang YH, Wang PH. Anxiety for procedures or anxiety for results. *J Chin Med Assoc* 2020;**83**:626–7.