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Taiwanese Journal of Obstetrics & Gynecology

journal homepage: www.tjog-online.com

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Clinical trial should be more rigorous



Recently, Dr. Pedro T. Ramirez et al. has published an article in the *New England Journal of Medicine* (NEJM) titled “Minimally Invasive versus Abdominal Radical Hysterectomy for Early- Stage Cervical Cancer LACC Clinical Trial” [1]. The article has caused public controversy worldwide, since there is discrepancy between the results of this study and the majority of published researches [2–8]. Dr. Pedro T. Ramirez’s article produces man-bites-dog effect because the results of this article are at variance with the majority. However, clear bias shown in the trial renders this article unsound. Therefore, TAMIG has responsibility for releasing a statement as follows:

1. TAMIG (Taiwan Association for Minimally Invasive Gynecology) has opposing views towards the conclusion from the articles published in the *New England Journal of Medicine* (NEJM) titled “Minimally Invasive versus Abdominal Radical Hysterectomy for Early- Stage Cervical Cancer LACC Clinical Trial” and “Survival after Minimally Invasive Radical Hysterectomy for Early-Stage Cervical Cancer.” According to international expert and our reviews, outcomes for both minimally invasive surgery and laparotomy are comparable, while minimally invasive surgery raises healthcare quality.
2. This trial contains bias as the study design neglects critical aspects including the surgical competence and experience of the participating surgeons and standardization of the operation procedures, thereby impacting the study results. The LACC trial must take into consideration the surgical proficiency and experience of the surgeons involved as well as the standardization of the operation procedures with more discretion.
3. The number of operations and a surgeon’s surgical dexterity influence the quality of oncology treatment and outcome. Regrettably, the investigators in this trial recruited on average 2.1 cases per year per participating hospital site, rendering the study design and the method of evaluating surgical treatment outcomes questionable. Minimally invasive radical hysterectomy for the treatment of cervical cancer demands a high level of surgical dexterity, proficiency, and accumulated experience owing to the level of difficulty of this type of surgery. Thus, it is without a doubt that an inexperienced surgeon or an amateur will negatively impact the surgical outcome and result in a poor prognosis. Consequently, the technical variability of each participating surgeon is a serious confounding factor that should be subjected to further scrutiny.
4. To date, minimally invasive surgery for radical hysterectomy has yet to be standardized worldwide, and the surgical experience for minimally invasive radical hysterectomy in each country varies greatly. Furthermore, in this trial, each participating site was only required to submit outcomes from ten laparoscopic radical hysterectomies from a portion of surgeons who were willing to enroll in this trial. The discrepancy in surgical

competency as well as the lack of standardized operation procedure suggests performance bias and a flaw in study design and concept formation.

5. Poor methodologic quality and study selection lead to inaccurate and invalid outcomes. The investigators ought to know the disparity of surgical competency and experience of the surgeons as a large confounding factor. This lack of discretion in study selection results in erroneous outcomes, thereby interfering with the rights of patients to choose minimally invasive surgery.
6. Considerable innovations and breakthroughs have been achieved in the development of laparoscopic surgeries with respect to surgical techniques and mentality. Surgical methods and instruments are continuously being refined, and researches to date have shown the breadth of benefits of minimally invasive surgery. These advantages should not be overlooked or tarnished. Thus, the results from this trial should not be overemphasized; instead, extensive analyses and research efforts are compulsory.
7. TAMIG strongly advocates minimally invasive surgery for the treatment of endometrial cancer. As for the treatment of cervical cancer, detailed discussion and counselling to the patient should be offered and provided. Should the patient choose minimally invasive surgery for treatment of cervical cancer, she should be allowed and subjected to this operation by a qualified and experienced surgeon.

Finally, minimally invasive surgery indeed provides a new vision in the patient’s care, because undeniable evidence has suggested the life quality and outcomes of minimally invasive therapy is much better than laparotomy not only for benign tumor but also for endometrial cancer [9–12].

Acknowledgment

We are grateful to the board of directors of TAMIG for their valuable opinions on this manuscript after eight-time discussions at TAMIG board meetings.

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