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อัญเชิญพระราชดำรัสพระราชทานแก่สูตินรีแพทย์ทั่วประเทศ

ปีนี้ นับเป็นสิริมงคลสูงสุดของสูตินรีแพทย์ทั่วประเทศทุกท่านครับ เนื่องด้วย สมเด็จพระกนิษฐาธิราชเจ้า กรมสมเด็จพระเทพรัตนราชสุดา ฯ สยามบรมราชกุมารี ได้ทรงพระกรุณาโปรดเกล้าโปรดกระหม่อม พระราชทานพระราชดำรัสเนื่องในโอกาสที่ราชวิทยาลัยสูตินรีแพทย์แห่งประเทศไทย ดำเนินการครบ 50 ปี เพื่อเป็นสิริสวัสดิ์พิพัฒนมงคล และเป็นขวัญกำลังใจกับสูตินรีแพทย์ทั่วประเทศ ตามที่คณะผู้บริหารราชวิทยาลัย ฯ ได้ทำหนังสือกราบบังคมทูลเกล้า ฯ ขอพระราชทาน และได้ทำพิธีรับมอบแผ่นวีดิทัศน์พระราชดำรัส ณ สำนักงานราชวิทยาลัย ฯ เมื่อวันที่ 23 กันยายน พ.ศ. 2564 และได้พระราชทานวโรกาสให้คณะผู้บริหารราชวิทยาลัยสูตินรีแพทย์แห่งประเทศไทย เข้าเฝ้าเพื่อถวายรายงาน และทูลเกล้าฯ ถวายเงินโดยเสด็จพระราชกุศล ตามพระราชอัธยาศัย เมื่อวันที่ 7 ธันวาคม 2564

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Aim and Scope of the Thai Journal of Obstetrics and Gynaecology (Official journal of the Royal Thai College of Obstetricians and Gynaecologists (RTCOG)

Thai Journal Obstetrics and Gynaecology (TJOG) is the official journal of The Royal Thai College of Obstetricians and Gynaecologists (RTCOG). This is a double-blind peer-reviewed journal aiming to promote academic knowledge and provide a forum for publication in Obstetrics and Gynecology. Manuscripts submitted to TJOG will be accepted on the understanding that the author must not have previously submitted the paper to another journal or have published the material elsewhere.

Type of Paper: Special (invited) article, Original article, Case report
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Peer Review Process

TJOG has double-blind peer-review process. The editorial board consists of professor, associate professor and assistant professor in fields of Obstetrics and Gynaecology, who have experience in conducting and publishing research. At least two reviewers evaluate manuscript. Initial reviews usually accomplish within 4 weeks.

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RTCOG

Journal History

TJOG is the official journal of RTCOG. This is a double-blind peer-reviewed journal aiming to promote academic knowledge and provide a forum for publication in Obstetrics and Gynecology. First issue of TJOG (Volume 1) was published in June 1989.

Improvement of TJOG has been documented. TJOG was accepted for indexing by the Thai Journal Citation Index (TCI) in December 2010 and indexed in the ASEAN Citation Index (ACI) in September 2015. TJOG also received the National Journal Award from the 3rd TCI-Scopus-TRF Journal Awards on December 15, 2016.

Direction to contributors. All papers should be sent to Editor, Thai Journal of Obstetrics and Gynaecology by online submission. The editorial board will decide upon the time of publication and retain the right to modify the style and the length of the contribution. However, major changes will be agreed with the authors.

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Manuscripts of original work should be arranged in the conventional order of title page, abstract, keywords, introduction, materials and methods, results, discussion, acknowledgments, references, table and figure legends.

Manuscripts of research article, case report and review article (without author's name) will be reviewed by two reviewers. Editor in chief will make the final decision in case of discrepancy of reviewer's opinion. The editorial board has the right to grammatically correct any content and has all right preserved to consider and to publish any article.

All published manuscripts are properties of TJOG. The content and any opinions in the published papers are the sole responsibility of the authors, not the editorial board.

Title page. The title page should contain the title, which should be concised and informative, the authors' name with

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Abstract. A structured abstract, with 250 words or less, is submitted as required for regular articles. The abstract should state the Objective, Materials and Methods, Results, and Conclusion, each with a brief adequate presentation. Abstracts for case reports should not exceed 250 words.

Keyword. Below the abstract list 3 to 5 keywords or short phrases for indexing purposes.

Introduction. State clearly the purpose of the study. Summarize the rationale for the study. Give only strictly pertinent references and it is not necessary to include all the background literature.

Materials and Methods. Describe briefly the plan, patients, procedures, controls and statistical method employed.

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Example of references:

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Phupong V, Aribarg A. Congenital arteriovenous malformations of the uterus. Thai J Obstet Gynaecol 2000;12:67-70.

Book

Cunningham FG, Leveno KJ, Bloom SL, Hauth JC, Rouse DJ, Spong CY. Williams Obstetrics. 23rd ed. New York: McGraw-Hill, 2010: 804-31.

Chapter in a Book

Phupong V. Management of PPROM AT 32 to 34 weeks. In: Desai SV, Tank P, eds. Handbbok on preterm prelabor rupture of membranes in a low source setting. New Delhi: Jaypee Brothers Medical Publishers Ltd, 2012: 39-46.

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Publication Ethics and Publication Malpractice Statement.

The publication ethics is required for publication in TJOG (Thai J Obstet Gynaecol). The publication ethics guidelines are guided by the Committee on Publication Ethics-(COPE).

Editors of Thai Journal of Obstetrics and Gynaecology

- attempt to meet the demand of readers and authors, improve the quality of the journal, and have processes in place to assure the quality of the material published, seek the opinions of authors, readers, reviewers and editorial board members about the ways to improve the journal's processes and maintain the integrity of the academic record and preclude business needs from intellectual and ethical standards.
- have a duty to act if editors suspect misconduct or if a misconduct is documented, pursue misconduct for the following reasons in published and unpublished work: plagiarism, data fabrication and falsification, when a submitted article has been found to be under revision elsewhere or published elsewhere, or where there is citation manipulation, and are willing to publish corrections, clarifications, retractions and apologies when needed.
- seek assurances that all research has been approved by research ethics committee or institutional review board, and ensure that research published was carried out according to the relevant internationally accepted guidelines such as the Declaration of Helsinki for clinical research
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- confirm that the authorship of research publications accurately reflect authors' contributions to the work and

reporting, and disclose sources of funding and conflicts of interest.

- present the research conducted in an ethical and responsible manner and comply with all relevant legislation, describe the methods clearly so that the findings can be confirmed by others, present the results clearly, honestly, and without fabrication, falsification or inappropriate data manipulation.

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- have objective and constructive comments in their reviews, and provide the journals with personal and professional information that is accurate from their expertise

Publication Decisions

Thai Journal of Obstetrics and Gynaecology will not accept articles which have been published (except in the form of an abstract) or are being considered for publication by another journal. Papers being considered for publication here should not be submitted to other journals.

The editor of Thai Journal of Obstetrics and Gynaecology is responsible for deciding which of the articles submitted to the journal should be published. The editor may be guided by the policies of the journal's editorial board and constrained by such legal requirements regarding libel, copyright infringement and plagiarism. The editor may confer with editorial board or reviewers in making this decision.

Plagiarism

Intellectual property is seriously concerned by TJOG. On submission, all articles are screened using the 'HelioBLAST' (https://helioblast.heliotext.com). Any plagiarism is unacceptable. The Editor-in-Chief will be informed. Plagiarism results in rejection. If plagiarism is detected during reviewing process by any means, all the process will be immediately withheld. The Editor-in-Chief will contact the corresponding author and/or all authors for explanation. Rejection of submission will occur once the explanation is unsatisfactory. If plagiarism is detected after publication, the article will be retracted. All the authors' institutions will be contacted to explain the retraction and inform the expected future behaviours. The event of retraction will be officially announced in the Journal.

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Thai Journal of Obstetrics and Gynaecology
January 2022, Vol. 30, No. 1, pp. 1.

EDITORIAL

In the last year 2021, we had a very special opportunity to celebrate the 50th anniversary of the founding of the Royal Thai College of Obstetricians and Gynaecologists (RTCOG). Her Royal Highness Princess Sirindhorn Debaratanasuda gave a royal speech to Thai obstetricians and gynecologists in the 36th annual meeting of the RTCOG on the occasion of the 50th anniversary of the founding of the RTCOG. This royal speech makes happiness and gives encouragement to all of us.

At the beginning of New Year 2022, it's time for beginning good things. May this year bring happiness, new inspirations and new success to all members of RTCOG. Wish all of the RTCOG members and families safe from COVID-19.

Editor in Chief and managing staff of Thai Journal of Obstetrics and Gynaecology (TJOG) already attended "The 5th meeting of the project on system development and quality improvement of Thai journals in the Scopus database" on 23 December 2021 at Eastin Grand Hotel, Sathorn Rd, Bangkok, Thailand. Editorial Board of TJOG looks forward to continuously raising the quality of the TJOG.

We would like to thank past RTCOG executive board, past editor in chief, editorial board and staff, all members of RTCOG, and all researchers for their kind contribution and support to TJOG. We take this opportunity to acknowledge all reviewers who have contributed much effort in the evaluation of manuscripts submitted to TJOG during the year 2021.

This first issue of TJOG 2022 contains many interesting articles. One special article is "Journal Citation Metrics".

Happy New Year 2022

Prof. Vorapong Phupong, M.D.
Editor in Chief

Thai Journal of Obstetrics and Gynaecology
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SPECIAL ARTICLE

Journal Citation Metrics

Vorapong Phupong, M.D.*

** Department of Obstetrics and Gynecology, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand*

ABSTRACT

Journal citation metrics are the journal ranking indicator measured by how many times of a journal article is cited by other articles, books, or authors. There have many journal citation metrics for evaluation of journal ranking. The examples of journal citation metrics include journal impact factor, CiteScore, SCImago Journal Rank, *h*-index and Quartile journal ranking. Thai Journal Obstetrics and Gynaecology is the official journal of The Royal Thai College of Obstetricians and Gynaecologists. Thai Journal Obstetrics and Gynaecology has been accepted for inclusion in the Scopus database since July 2019. Thai Journal Obstetrics and Gynaecology also received the Q4 journal rankings (SJR score 0.12) in Obstetrics and Gynaecology category from Scimago Journal & Country Rank 2020.

Keywords: journal impact factor, CiteScore, SCImago Journal Rank, h-index, Quartile journal ranking

Correspondence to: *Vorapong Phupong, M.D. Placental Related Diseases Research Unit, Department of Obstetrics and Gynecology, Faculty of Medicine, Chulalongkorn University, Rama IV Road, Pathumwan, Bangkok 10330, Thailand. Email: vorapong.p@chula.ac.th*

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Journal citation metrics are the journal ranking indicator measured by how many times of a journal article is cited by other articles, books, or authors[1]. It is usually used as an indicator for the relative importance of a journal within its field. Higher citation metrics scores journals are given status of being more important, or carry more prestige in their respective fields, than journals with lower scores. It is used by an institute to give a promotion or hiring. It is also used by authors in guiding which journal to publish in. There have many journal citation metrics for evaluation of journal ranking. In this article, some citation metrics are described.

Type of citation metrics

1. Impact factor (IF)

IF is the last two-year average ratio of citations to articles published in each journal. It is indexed by Clarivate's Web of Science[2].

IF was originated by Eugene Garfield, the founder of the Institute for Scientific Information (ISI) in Philadelphia. IF started from year 1975 for journals listed in the Journal Citation Reports (JCR). ISI was obtained by Thomson Scientific and Healthcare in year 1992, and it was known as Thomson ISI. In year 2018, Thomson-Reuters sold ISI to Onex Corporation and Baring Private Equity Asia. And they founded a new

corporation, Clarivate, which is now the publisher of the JCR[3].

IF of a journal is calculated by dividing the number of current year citations to the source items published in that journal during the previous two years (Fig. 1).

X = total citations in year 2020
Y = year 2020 citations to articles published in year 2018-2019
Z = number of articles in year 2018-2019
Year 2020 impact factor = Y/Z

Fig. 1. Journal impact factor calculation.

For example, one journal had 637 and 565 citations in year 2018 and 2019, respectively, and had 38 and 39 articles in year 2018 and 2019, respectively. Thus, the calculation of impact factor of this journal is as follows:

IF = (637 + 565) / (38 + 39) = 15.61

2. CiteScore (CS)

CS is a measurement of an academic journal indicating the yearly average number of citations to recent articles published in the journal. CS was started to use in December 2016 by Elsevier as an alternative to the generally used JCR IF. CS is based on the citations that indexed in the Scopus database. CS is collected for articles published in the previous 4 years. CS is calculated from the number of citations, received in that year and past 3 years, for articles published in the journal during that 4-year period, divided by the total number of published documents (articles, book chapters, reviews, data papers, and conference papers) in that journal during the same 4-year period[4]. (Fig. 2).

$$CS_{2020} = \frac{Citation_{2020} + Citation_{2019} + Citation_{2018} + Citation_{2017}}{Publications_{2020} + Publications_{2019} + Publications_{2018} + Publications_{2017}}$$

Fig. 2. Journal impact factor calculation.

For example, Thai Journal of Obstetrics and Gynaecology had 6 citations during 2017-2020 and 59 published articles during 2017-2020. Thus, CS_{2020} of Thai Journal of Obstetrics and Gynaecology was 0.1.

The differences between IF and CS are shown in Table 1.

Table 1. The difference between Impact Factor and CiteScore[5].

	Impact Factor	**CiteScore**
Total years of evaluation	2	4
Database	Journal Citation Reports	Scopus
Company	Clarivate's Web of Science	Elsevier
Evaluated publications	Articles and reviews	All

3. SCImago Journal Rank (SJR)

SJR is originated by Scimago Lab. It was launched from a research group at University of Granad. SJR is a measurement of the scientific influence of

scholarly journals that accounts for both the number of citations received by a journal and the prestige or importance of the journals where the citations come from. It is indexed in Scopus database (Elsevier). A SJR is a numeric score indicating the average number of weighted citations received during a selected year per article published in that journal during the past 3 years. Higher scores indicate greater journal prestige. Journals can be grouped by subject area (27 major thematic areas), subject category (313 specific subject categories) or by country. Citation data is drawn from over 34,100 titles from more than 5,000 international publishers and country performance metrics from 239 countries worldwide[6].

4. h-index

The *h*-index is defined as the maximum value of *h* such that the journal/given author has published at least *h* articles that have each been cited at least *h* times (Fig. 3)[7].

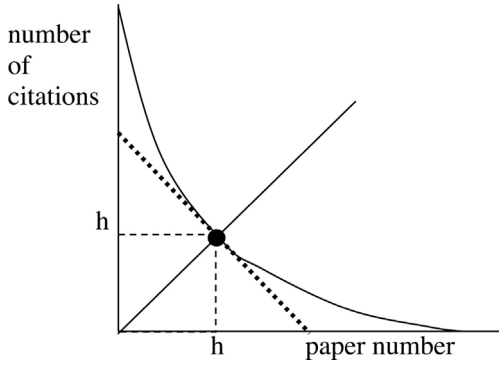

Fig. 3. The *h*-index[7].

The *h*-index was originated in 2005 by Jorge E. Hirsch, a physicist at UC San Diego. It was used as a tool for ascertaining theoretical physicists' relative quality. It is sometimes called the Hirsch number or Hirsch index[7]. Hirsch purposed the *h*-index to address the main disadvantages of other bibliometric indicators. The total number of articles metric does not account for the quality of scientific publications. The total number of citations metric can be heavily affected by participation in a single publication of major influence (for example, methodological articles proposing new techniques or methods, which can create a lot of citations). The *h*-index is aimed to measure simultaneously the quantity and quality of scientific output[7]. Currently, the *h*-index has been used in many databases such as ISI Clarivate's Web of Science, Scopus database from Elsevier, and Google Scholar.

For example, Thai Journal of Obstetrics and Gynaecology has an *h*-index of 1. It means 1 articles of this journal have more than 1 number of citations.

5. Quartile journal ranking

Quartile journal ranking is another type of measurement used for evaluation of journals. Quartile is used by ISI Clarivate's Web of Science, and Scopus database from Elsevier.

The quartiles journal ranking rank the journals from highest to lowest based on their impact factor or impact index. There are four quartiles: Q1, Q2, Q3 and Q4 (Table 2). The most prestigious journals within a subject area are those occupying the first quartile, Q1[8].

For example, Thai Journal Obstetrics and Gynaecology was in the 153rd order of 181 journal in Obstetrics and Gynaecology category from Scimago Journal & Country Rank 2020. Thus, Thai Journal Obstetrics and Gynaecology was in Q4 journal rankings.

Table 2. Quartile journal ranking[8].

Q1 is occupied by journals in the top 25% group
Q2 is occupied by journals in the 25 to 50% group
Q3 is occupied by journals in the 50 to 75% group
Q4 is occupied by journals in the 75 to 100% group

Citation metrics of Thai Journal of Obstetrics and Gynaecology

The Association of Obstetricians and Gynecologists of Thailand was approved to register as a legal association on March 5, 1970. The Association of Obstetricians and Gynecologists of Thailand was changed to the Thai College of Obstetricians and Gynaecologists in 1987, and has been received in the royal patronage as the Royal Thai College of Obstetricians and Gynaecologists (RTCOG) since 1993. This year is 50 years anniversary of founding of RTCOG. Thai Journal Obstetrics and Gynaecology is the official journal of RTCOG. First issue of Thai Journal of Obstetrics and Gynaecology (Volume 1) was published in June 1989. Thai Journal of Obstetrics and Gynaecology had 2 issues in the first year of publication. Thai Journal Obstetrics and Gynaecology was indexed in Index Medicus from Institute De L' Informatifique Et Technique from 1989 to 1997. Currently, Thai Journal Obstetrics and Gynaecology has 6 issues per year and on volume 29 in year 2021. Thai Journal Obstetrics and Gynaecology has been indexed in the Thai Journal Citation Index (TCI), the ASEAN Citation Index (ACI), the directory of open access journals (DOAJ), EuroPub, and Google Scholar[9].

Thai Journal of Obstetrics and Gynaecology has already been accepted for inclusion in the Scopus database since July 2019. Thai Journal of Obstetrics and Gynaecology also received the Q4 journal rankings (SJR score 0.12) in Obstetrics and Gynaecology category from Scimago Journal & Country Rank 2020[10] (Fig. 4).

Fig. 4. Scimago Journal & Country Rank 2020 of Thai Journal of Obstetrics and Gynaecology[11].

Conclusion

In conclusion, journal citation metrics are the journal ranking indicator measured by how many times of a journal article is cited by other articles, books, or authors. Journal citation metrics are used to compare the impact of journal. It is usually used by authors to find the journal for publication. There have many journal citation metrics for evaluation of journal ranking. Each

journal citation metric has different methods of evaluation.

Potential conflicts of interest

The author declares no conflicts of interest.

References

1. Garfield E. Citation indexes for science; a new dimension in documentation through association of ideas. Science 1955;122:108-11.
2. Waltman L, Traag VA. Use of the journal impact factor for assessing individual articles: Statistically flawed or not? F1000Res 2020;9:366.
3. https://clarivate.com/webofsciencegroup/essays/impact-factor.
4. https://journalmetrics.scopus.com
5. Van Noorden R. Controversial impact factor gets a heavyweight rival. Nature 2016;540:325-6.
6. SCImago, (n.d.). SJR - SCImago Journal & Country Rank [Portal]. Retrieved 10 December 2021, from http://www.scimagojr.com
7. Hirsch JE. An index to quantify an individual's scientific research output. Proc Natl Acad Sci U S A 2005;102:16569-72.
8. https://www.mondragon.edu/en/web/biblioteka/publications-impact-indexes
9. https://he02.tci-thaijo.org/index.php/tjog/about
10. Phupong V. Editorial. Thai J Obstet Gynaecol 2021;29:185.
11. https://www.scimagojr.com/journalsearch.php?q=thai+journal+of+obstet+gynaecol

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OBSTETRICS

Effects of Episioguide – a 60° Mediolateral Episiotomy Guide Device – on Post Suture Episiotomy Angle: A randomized controlled trial

Chatsaran Thanapongpibul, M.D.*,
Maysita Suksamarnwong, M.D.*

** Department of Obstetrics and Gynaecology, Faculty of Medicine, Srinakharinwirot University, HRH Princess Maha Chakri Sirindhorn Medical Center, Nakhon Nayok, Thailand*

ABSTRACT

Objectives: To compare the post-suture episiotomy angle between groups on which the Episioguide – a 60° mediolateral episiotomy (MLE) guide device was used and not used in the performance of MLE.

Materials and Methods: This prospective randomized controlled trial was conducted at the HRH Princess Maha Chakri Sirindhorn Medical Center, Nakhon Nayok, Thailand. Eligible women were randomized into two groups, the first group was women who had a MLE using the Episioguide and the second group was women who had a conventional MLE. The primary outcome was a comparison of the rates of post-suture episiotomy angle in the safe zone (30°-60°) between the groups.

Results: One-hundred and twelve eligible pregnant women were recruited, of whom 88 underwent randomization, 44 each in the Episioguide and conventional MLE groups. The procedures using the Episioguide had a significantly higher rate of a post-suture episiotomy angle in the desired 30°-60° range (relative risk (RR) 1.526, 95% confidence interval (CI) 1.023-2.277, p = 0.032), and there was a statistically significant difference in mean post suture angle between the two groups, 34.636° ± 9.445° in the Episioguide group and 27.614° ± 9.267° in the standard procedure group (mean difference 7.022, 95%CI 3.057-10.988, p = 0.001).

Conclusion: Using the Episioguide to perform a MLE achieved a significantly higher rate of post-suture episiotomy angle in the safe zone compared with conventional MLE.

Keywords: episiotomy, episioguide, angle of incision, obstetrical anal sphincter injuries (OASIS), post-suture angle.

Correspondence to: *Maysita Suksamarnwong, M.D., Department of Obstetrics and Gynaecology, Faculty of Medicine, Srinakharinwirot University, HRH Princess Maha Chakri Sirindhorn Medical Center, Nakhon Nayok 26120, Thailand. E-mail: maysita078@hotmail.com*

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ผลของการใช้เครื่องมือช่วยตัดฝีเย็บ Episioguide ในการตัดฝีเย็บชนิด mediolateral episiotomy ต่อมุมหลังเย็บแผลฝีเย็บ: การทดลองแบบสุ่มและมีกลุ่มควบคุม

ชัชศรัณย์ ธนพงษ์พิบูล, เมสิตา สุขสมานวงศ์

บทคัดย่อ

วัตถุประสงค์: *เพื่อเปรียบเทียบมุมหลังการเย็บซ่อมฝีเย็บในมารดาที่ได้รับการตัดฝีเย็บชนิด mediolateral episiotomy (MLE) ด้วยการใช้เครื่องมือ Episioguide กับมารดาที่ไม่ได้ใช้เครื่องมือช่วยตัดฝีเย็บ*

วัสดุและวิธีการ: *การศึกษานี้เป็นการศึกษาแบบสุ่มซึ่งเก็บข้อมูลที่โรงพยาบาลศูนย์การแพทย์สมเด็จพระเทพรัตนราชสุดา ฯ สยามบรมราชกุมารี จังหวัดนครนายก โดยทำการแบ่งกลุ่มมารดาเป็น 2 กลุ่ม ได้แก่ กลุ่มที่ได้รับการตัดฝีเย็บแบบ MLE ด้วยการใช้ Episioguide และกลุ่มที่ไม่ได้ใช้เครื่องมือช่วย และทำการเปรียบเทียบมุมฝีเย็บหลังการเย็บซ่อมที่อยู่ในระยะปลอดภัย คือ ช่วง 30 ถึง 60 องศาในแต่ละกลุ่ม*

ผลการศึกษา: *มารดาตั้งครรภ์จำนวน 88 คนจาก 112 คนได้รับการแบ่งกลุ่มแบบสุ่มเป็น 2 กลุ่ม กลุ่มละ 44 คน คือ กลุ่มที่ได้รับการตัดฝีเย็บแบบ MLE ด้วยการใช้ Episioguide และกลุ่มที่ไม่ได้ใช้เครื่องมือช่วย พบว่ากลุ่มที่ใช้ Episioguide วัดมุมหลังการเย็บฝีเย็บอยู่ในระยะปลอดภัยมากกว่า (relative risk (RR) 1.526, 95%confidence interval (CI) 1.023-2.277, p = 0.032) และมีค่าเฉลี่ยของมุมหลังการเย็บฝีเย็บที่แตกต่างกันอย่างมีนัยสำคัญทางสถิติ (mean difference 7.022, 95%CI 3.057-10.988, p = 0.001).*

สรุป: *มารดาที่ได้รับการตัดฝีเย็บโดยใช้เครื่องมือ Episioguide มีมุมหลังการเย็บฝีเย็บอยู่ในช่วงปลอดภัยมากกว่ากลุ่มที่ไม่ได้ใช้เครื่องมือช่วยอย่างมีนัยสำคัญทางสถิติ*

คำสำคัญ: *การตัดฝีเย็บ, Episioguide, มุมของฝีเย็บ, การบาดเจ็บของหูรูดทวารหนัก*

Introduction

An episiotomy is the incision made along the perineum during the second stage of labor to enlarge the opening for the baby to pass through. There are two main types of episiotomy: midline and mediolateral episiotomy (MLE). A midline episiotomy begins at the posterior fourchette, makes a 2-3 cm incision along the midline of the perineum, ending well before the external anal sphincter, while the MLE also begins at the midline of the fourchette but extends down either to the right or left direction at a 60-degree angle to the midline[1]. The midline episiotomy has a higher tendency of leading to obstetrical anal sphincter injuries (OASIS)[2], which is a severe perineal laceration after vaginal delivery that extends into or through the anal sphincter complex[3]. An OASIS leads to higher risk of wound complications during the early postpartum period (i.e. one study reported 19.8% of wound infections and 24.6% of subsequent wound breakdowns during the first 6 weeks postpartum were related to the episiotomy), is a common cause of fecal incontinence and increased postpartum perineal pain[3-5]. Regarding\OASIS, the recent meta-analysis found no statistically significant between non-episiotomy and selective episiotomy[6]. However, the World Health Organization (WHO) has recommended the restrictive use of episiotomy. If an episiotomy is required to assist delivery, the mediolateral episiotomy is preferred[7].

There is limited evidence regarding clinical outcomes from different incision angles in MLE. Eogan et al reported that every 6° away from the perineal midline decreased the risk of third-degree tear by 50%[8]. Stedenfeldt et al found that scarred episiotomy angle ranging from 30°-60° was significantly associated with less risk of OASIS[9].

Interestingly, it has been reported that a 60° MLE incision angle resulted in suture angles of 32°-59° and a low incidence of anal sphincter tearing, anal incontinence and perineal pain[10]. However, currently even when physicians attempt to perform an MLE, only 15% of the incisions are made within the desired 58-62° range[11]. Given this low range of accurate performance of the MLE, a technique to accurately create a 60° incision angle 60° would be beneficial for clinical outcomes.

The Episcissors-60® (Medinvent, United Kingdom) is a tool for right-handed users, which was modified from surgical scissors to achieve a 60° incision angle in MLEs by adding a 60° angled guide limb to the blades[12]. A previous randomized trial found that post suture episiotomy angles when using the Episcissors-60® were much further than 60 degrees and had a lower risk of OASIS[13-16]. However, the cost of a reusable Episcissors-60® is 400 British Pounds, approximately 16,000 Thai Baht, which is too expensive for many hospitals in developing countries to add to their routine equipment.

Given these considerations, for the present study, we developed a device we call the Episioguide a cheaper Episcissors-alternative stainless-steel medical device to be used in MLEs to achieve a more precise 60° incision angle. This device can be placed on the perineum during fetal head crowning to guide an accurate 60° incision angle. To determine the accuracy of the Episioguide, we compared the post-suture episiotomy angle between groups on which the Episioguide was used and not used in the performance of MLE.

Materials and Methods

This prospective randomized controlled trial (RCT) was approved by the Strategic Wisdom and Research Institute of Srinakharinwirot University (certificate number: SWUEC/F-341/2561) and registered at the Thai Clinical Trials registry (TCTR identification number: TCTR20190924002). The participants were recruited at the labor room at HRH Princess Maha Chakri Sirindhorn Medical Center (MSMC), Faculty of Medicine, Srinakharinwirot University, Ongkharak, Nakhon Nayok, Thailand between March and September 2019. All singleton low risk term pregnant women who planned for vaginal delivery were considered to be eligible for this study and required to sign a written informed consent form. The exclusion criteria were (1) women in whom an episiotomy was not required, (2) women who delivered by operative vaginal delivery, (3)

women who had an emergency caesarean section, and (4) women who declined to participate.

If an episiotomy was required, the participant was randomized during the second stage of labor prior to making the incision into two groups using a block randomization list (block size 4) from www.sealedenvelope.com, the participants in the first group were assigned to receive a MLE using the Episioguide and all in the second group received a conventional MLE.

The MLEs were performed by 12 residents of Department of Obstetrics and Gynaecology, Faculty of Medicine, Srinakharinwirot University. They were trained to use the Episioguide with at least 50 paper models by placing the Episioguide at a picture of the perineum during fetal head crowning at the proper position before performing MLE prior to the beginning of the study.

The Episioguide is a stainless-steel medical device which is designed to guide an MLE to achieve a 60° incision angle. As shown in Fig. 1, the Episioguide consists of 3 main parts, a shank, guide-limb and clip. The shank is the core of the device. The guide-limb is designed to make an angle of 60° with the shank. The clip is located at the back of the device and used to make a tight connection between the device and the perineum. We designed the Episioguide to be suitable for both right and left MLEs. Its edge is blunt in order to prevent perineal trauma. Since it is reusable, sterilization is required prior to every use of the device.

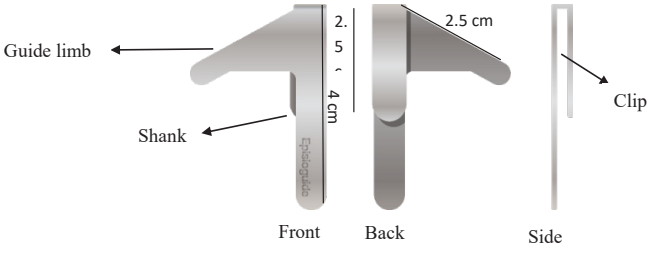

Fig. 1. A labeled schematic illustration of Episioguide.

Using the Episioguide at the time of fetal head crowning, place it at the perineum as shown in Fig. 2.

1. Align the position of the shank to be vertically in line with the perineal midline and pointed toward the anus
2. Tightly fasten the clip to the perineum
3. Use either Mayo or episiotomy scissors to perform either a left or right MLE next to the guide-limb at a 60° angle

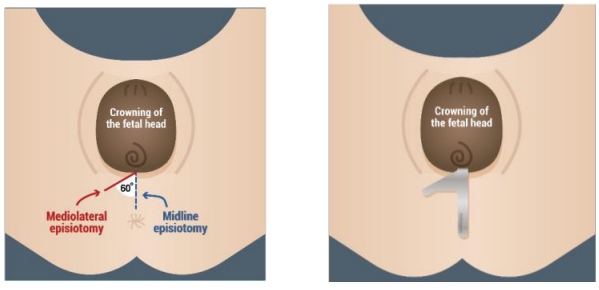

Fig. 2. Illustrative diagram of mediolateral episiotomy (MLE) and midline episiotomy (left) and the use of Episioguide in MLE (right).

The primary outcome of the study was post suture episiotomy angle in the safe zone of 30°-60°. The measurements were taken immediately after the perineorrhaphy with the patient in the lithotomy position with both legs flexed at the hip joints. The angle in relation to the midline was measured by drawing lines onto a translucent plastic sheet placed over the perineum, using a standard protractor. The measurements were done by another obstetric trainee (C.T.) who was blinded to all identifying participant details and group. Apart from the post suture episiotomy angle, the occurrence of third or fourth degree perineal tears was an additional parameter considered in this study.

The sample size required to compare two independent group proportions was calculated using the power of 80%. We expected that 80% and 50% of patients from the Episioguide and conventional groups, respectively, would receive the incision which would result in a post suture angle between 30° and 60° with 95% confidence intervals. From the calculation, 40 women were required in each trial group. Allowing for 10% missing data, we set an overall recruitment goal of 88 women.

Data analysis was performed with IBM SPSS statistics version 22. All data were tested for normal distribution by the Shapiro-Wilk test. The demographic data were presented as mean and standard deviation, median and interquartile range or number and percentage. The proportions of women with a post suture episiotomy angle in the range of 30° to 60° between the two groups were compared with chi square test. The mean post suture episiotomy angle was compared with independent t test. The significance level was set at $p < 0.05$.

Results

During the study period, March-September 2019, one hundred and twelve eligible pregnant women were recruited, of whom twenty-four were excluded, leaving eighty-eight women to undergo randomization. Forty-four pregnant women were assigned to receive MLE using the Episioguide and the remaining 44 participants were assigned to receive conventional MLE as shown in Fig. 3.

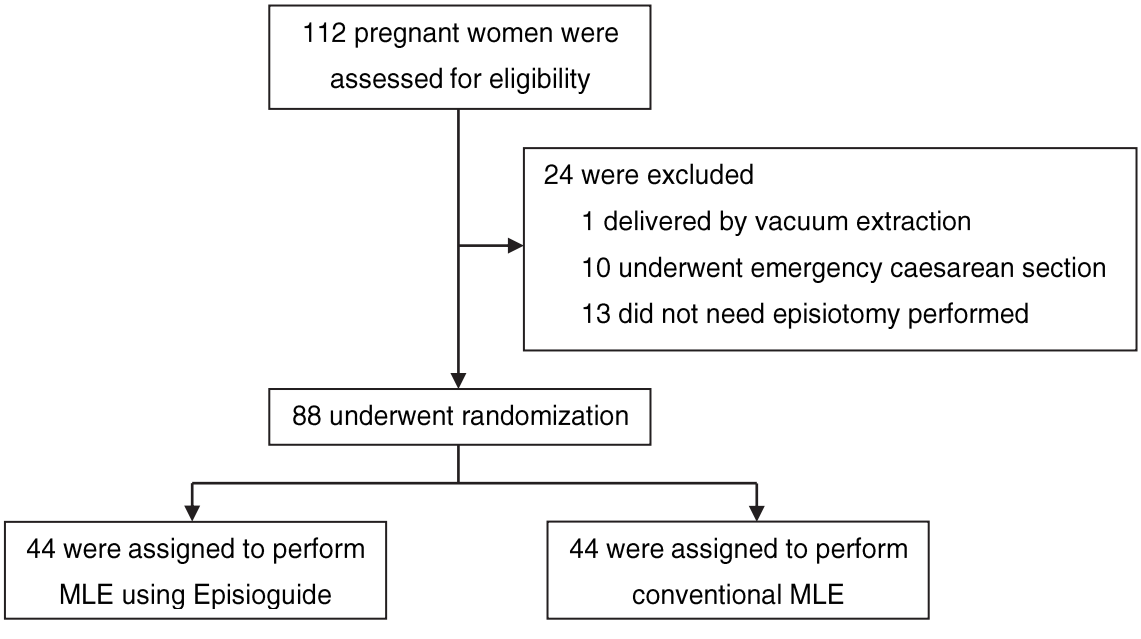

Fig. 3. The flow chart of clinical trial enrollment and randomization.

There were no statistically significant differences in baseline characteristics between the two groups (Table 1).

The study found a significant difference between the groups regarding the number of cases achieving a safe post suture episiotomy angle (30°-60°), in which 29 and 19 participants in the Episioguide and conventional groups, respectively (65.9% vs 43.2%, relative risk (RR) 1.526, 95% confidence interval (CI) 1.023-2.277, p = 0.032) (Table 2).

Table 1. Baseline characteristics of the participants.

	Episioguide (n = 44)	Conventional MLE (n = 44)	p value
Maternal characteristics			
Age [median (IQR)] years	23 (22-29)	26 (23.5-30.5)	0.066[2]
Parity			
0 [n (%)]	20 (46.5)	23 (53.5)	0.185[3]
1 [n (%)]	22 (57.9)	16 (42.1)	
2 [n (%)]	1 (16.7)	5 (83.3)	
3 [n (%)]	1 (100)	0 (0)	
GA [median (IQR)] weeks	39 (38-39)	39 (38-39)	0.791[2]
BMI [median (IQR)] kg/m^2	21.65 (19.9-24.2)	22.25 (20.1-23.95)	0.625[2]
Weight gain			
Poor weight gain [n (%)]	18 (62.1)	11 (37.9)	0.277[3]
Normal weight gain [n (%)]	15 (42.9)	20 (57.1)	
Excessive weight gain [n (%)]	11 (45.8)	13 (54.2)	
Fetal characteristics			
BBW (mean ± SD) g	3195 ± 381.43	3125 ± 362.16	0.380[1]
HC (mean ± SD) cm	33.44 ± 1.39	33.58 ± 1.40	0.647[1]
Sex			
Female [n (%)]	16 (45.7)	19 (54.3)	0.513[3]
Male [n (%)]	28 (52.8)	25 (47.2)	
Episiotomy characteristic			
Length [median (IQR)] mm	30 (25.5-33)	30 (25.5-32)	0.484[2]

[1] independent t test, [2] Mann-Whitney U test, [3] chi square test

IQR: interquartile range, GA: gestation age, BMI: body mass index, BBW: birth bodyweight, HC: head circumference, SD: standard deviation

Table 2. Difference between groups regarding number of cases achieving safe post-suture episiotomy angle (30-60°).

	Not safe	Safe	RR	95% CI	p value
Episioguide [n (%)]	15 (34.1)	29 (65.9)	1.526	1.023 - 2.277	0.032
Conventional MLE [n (%)]	25 (56.8)	19 (43.2)			

*Analysis using chi square test. RR: relative risk, CI: confidence interval

There was also a statistically significant difference between the two groups in terms of mean post suture episiotomy angle (34.6° ± 9.4° vs 27.6° ± 9.3°, respectively, mean difference 7.0, 95%

CI 3.1-10.9, p = 0.001) (Table 3).

Most post suture angles in the used group were 30°-39° while in the conventional group were 20°- 29°. The length of the episiotomy was not significantly different between two groups (18-52 mm vs 20-39 mm, respectively, p = 0.484). There were no cases of third- or fourth-degree perineal tears in either group.

Table 3. Difference between groups regarding mean post-suture episiotomy angle.

	Episioguide (mean ± SD)	Conventional MLE (mean ± SD)	Mean difference	95% CI	p value
Angle (degree)	34.6 ± 9.4	27.6 ± 9.3	7.0	3.1-10.9	0.001

* Analysis using independent t test. CI: confidence interval, SD: standard deviation

Discussion

We designed and developed the Episioguide to be a simple, convenient, and inexpensive device to guide an accurate 60° incision in MLE. The following research was a first RCT aimed to compare post suture episiotomy angle between Episioguide-guided MLEs and conventional MLEs. We found that the Episioguide-guided group had a 1.5 times higher proportion of episiotomies that successfully achieved post suture angles of 30° - 60° when compared to the conventional group. In addition, the use of the Episioguide resulted in a significantly smaller mean range of post suture episiotomy angle when compared with the conventional MLE group.

The mean post suture angle in the Episioguide-MLE group was 34.636°, within the safe zone similar to previous studies which marked the 60° line with gentian-violet[10] and using the Episcissors-60®[12], which achieved post suture angles of 44.43° and 40.6°, respectively.

The previous studies had shown that the post suture episiotomy angle differs from the incision angle[10,17]. The reasons for the difference might relate to the difference between elasticity and collagen content of connective tissue of individuals.

According to the low incidence of OASIS, our sample size was too small to demonstrate the incidences of third- and fourth-degree perineal tears. We suggest that further multicenter RCT studies of the Episioguide with a larger sample size would be useful to study the effects of using the Episioguide on OASIS and other postpartum outcomes including postpartum perineal pain, urinary and fecal incontinence and sexual intercourse related problems.

Our study found that the use of the Episioguide could be helpful to accurately achieve post suture episiotomy angles in the range of 30° - 60° from the midline. This device is easy to use and is inexpensive and thus easily accessible for any hospital. The cost of a reusable Episioguide is only 400 Thai Baht while the cost of the commercially available device such as Episcissors-60® is 400 British Pounds, approximately 16,000 Thai Baht. Physicians or even medical students can use it to perform MLEs together with episiotomy scissors. The Episioguide is designed to be used for either left- or right-side MLEs. Therefore, we suggest the usage of the Episioguide in every case in which it is decided to perform an MLE especially in medical and midwifery training schools. For further study, using the Episioguide to practice achieving a 60° MLE in medical students and their satisfaction with device usage should be evaluated.

Conclusion

In this prospective RCT study, we conclude that using the Episioguide to perform MLEs can achieve a significantly higher rate of 30° - 60° post suture episiotomy angle than the conventional MLE. In addition, the use of the Episioguide resulted in a significantly lower mean range of post suture

episiotomy angle.

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Potential conflicts of interest

The authors declare no conflicts of interest.

References

1. Cunningham FG, Leveno KJ, Bloom SL, Dashe JS, Hoffman BL, Casey BM, et al. Williams Obstetrics. 25th ed. New York: McGraw-Hill 2018.
2. Sooklim R, Thinkhamrop J, Lumbiganon P, Prasertcharoensuk W, Pattamadilok J, Seekorn K, et al. The outcomes of midline versus medio-lateral episiotomy. Reprod Health 2007;4:10.
3. Lewicky-Gaupp C, Leader-Cramer A, Johnson LL, Kenton K, Gossett DR. Wound complications after obstetric anal sphincter injuries. Obstet Gynecol 2015;125:1088-93.
4. ACOG Practice Bulletin No. 165: Prevention and Management of Obstetric Lacerations at Vaginal Delivery. Obstet Gynecol 2016;128:e1-e15.
5. Norderval S, Nsubuga D, Bjelke C, Frasunek J, Myklebust I, Vonen B. Anal incontinence after obstetric sphincter tears: incidence in a Norwegian county. Acta Obstet Gynecol Scand 2004;83:989-94.
6. Pereira GMV, Hosoume RS, de Castro Monteiro MV, Juliato CRT, Brito LGO. Selective episiotomy versus no episiotomy for severe perineal trauma: a systematic review with meta-analysis. Int Urogynecol J 2020;31: 2291-9.
7. WHO recommendations on intrapartum care for a positive childbirth experience 2018.
8. Drusany Staric K, Lukanovic A, Petrocnik P, Zacesta V, Cescon C, Lucovnik M. Impact of mediolateral episiotomy on incidence of obstetrical anal sphincter injury diagnosed by endoanal ultrasound. Midwifery 2017;51:40-3.
9. Stedenfeldt M, Pirhonen J, Blix E, Wilsgaard T, Vonen B, Øian P. Episiotomy characteristics and risks for obstetric anal sphincter injuries: a case-control study. BJOG 2012;119:724-30.
10. Kalis V, Landsmanova J, Bednarova B, Karbanova J, Laine K, Rokyta Z. Evaluation of the incision angle of mediolateral episiotomy at 60 degrees. Int J Gynaecol Obstet 2011;112:220-4.
11. Naidu M, Kapoor DS, Evans S, Vinayakarao L, Thakar R, Sultan AH. Cutting an episiotomy at 60 degrees: how good are we? Int Urogynecol J 2015;26:813-6.
12. Sawant G, Kumar D. Randomized trial comparing episiotomies with Braun-Stadler episiotomy scissors and EPISCISSORS-60(®). Med Devices (Auckl) 2015;8: 251-4.
13. van Roon Y, Kirwin C, Rahman N, Vinayakarao L, Melson L, Kester N, et al. Comparison of obstetric anal sphincter injuries in nulliparous women before and after introduction of the EPISCISSORS-60(®) at two hospitals in the United Kingdom. Int J Womens Health 2015;7:949-55.
14. van Roon Y, Vinayakarao L, Melson L, Percival R, Pathak S, Pradhan A. Comparative study of episiotomy angles achieved by cutting with straight Mayo scissors and the EPISCISSORS-60 in a birth simulation model. Int Urogynecol J 2017;28:1063-6.
15. Koh LM, van Roon Y, Pradhan A, Pathak S. Impact of the EPISCISSORS-60 mediolateral episiotomy scissors on obstetric anal sphincter injuries: a 2-year data review in the United Kingdom. Int Urogynecol J 2020;31:1729-34.
16. Divakova O, Khunda A, Ballard PA. Episcissors-60™ and obstetrics anal sphincter injury: a systematic review and meta-analysis. Int Urogynecol J 2020;31:605-12.
17. Freeman R, Hollands H, Barron L, Kapoor D. Cutting a mediolateral episiotomy at the correct angle: evaluation of a new device, the Episcissors-60. Med Devices (Auckl) 2014;7:23-8.

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OBSTETRICS

Efficacy of Cold Gel Pack in Reducing Postoperative Pain in Cesarean Delivery at Sanpasitthiprasong Hospital: Randomized controlled trial

Patchareeya Siripanthong, M.D.*,
Piyawadee Wuttikonsammakit, M.D.*,
Parinya Chamnan, M.D., Ph.D.**

** Department of Obstetrics and Gynecology, Sanpasitthiprasong Hospital, Ubonratchathani, Thailand*
*** Cardiometabolic Research Group, Department of Social Medicine, Sanpasitthiprasong Hospital, Ubonratchathani, Thailand*

ABSTRACT

Objectives: To evaluate efficacy and safety of cold gel pack in adjunctive to standard pain control in reducing postoperative pain after Cesarean delivery

Materials and Methods: Between December 2019 and March 2020, 34 women who underwent Cesarean delivery under regional anesthesia with neuraxial opioid at Sanpasitthiprasong Hospital were recruited. They were randomized into two groups: 1) receiving adjunctive cold gel pack covering surgical wound at 2-hour postdelivery for 20 minutes (intervention group, n = 17) or 2) receiving standard pain control (control group, n = 17). Pain scores were assessed using visual analogue scale (VAS) at 2 hours (before intervention), 6 hours (4 hours after intervention) and 24 hours postdelivery. Data on additional analgesic drugs, possible complications, participant's satisfaction were recorded. Pain scores were compared between treatment groups using student t-test and occurrence of complications compared using chi-square test.

Results: With comparable initial pain score, intervention group had significantly lower postoperative pain at 6 hours after Cesarean delivery than control group (mean pain score ± standard deviation 3.53 ± 2.12 and 5.44 ± 1.56 respectively, p = 0.005), but there was no difference at 24 hours postdelivery. Patients in both groups required similar amount of additional analgesia. There were no significant differences between groups in postpartum hemorrhage, length of hospital stays and surgical wound infection. There were moderate and high patient satisfaction similarly observed for the two groups. No adverse effect from intervention happened in the intervention group.

Conclusion: Adjunctive cold gel pack was efficacious in reducing postoperative pain at 6 hours after Cesarean delivery without safety concerns.

Keywords: cold gel pack, postoperative pain, cesarean delivery.

Correspondence to: *Piyawadee Wuttikonsammakit, M.D., Department of Obstetrics and Gynecology, Sanpasitthiprasong Hospital, Ubonratchathani 34000, Thailand. E-mail: piyawadeemfm@yahoo.co.th*

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การศึกษาประสิทธิภาพของการใช้ถุงเจลให้ความเย็นในการลดระดับความปวดหลังผ่าตัดคลอดบุตรที่โรงพยาบาลสรรพสิทธิประสงค์: การศึกษาทดลองแบบสุ่มมีกลุ่มเปรียบเทียบ

พัชรีญา ศิริพานทอง, ปิยวดี วุฒิกรสัมมากิจ, ปริญญา ชำนาญ

บทคัดย่อ

วัตถุประสงค์: *เพื่อศึกษาประสิทธิภาพของการใช้ถุงเจลให้ความเย็นในการลดระดับความปวดหลังผ่าตัดคลอดบุตร*

วัสดุและวิธีการ: *หญิงตั้งครรหลังผ่าตัดคลอดบุตรที่โรงพยาบาลสรรพสิทธิประสงค์ อุบลราชธานี จำนวน 34 ราย ระหว่างวันที่ 18 ธันวาคม 2562 ถึง 18 มีนาคม 2563 โดยผู้เข้าร่วมการวิจัยทุกรายได้รับการระงับความรู้สึกโดยการฉีดยาชาและยาแก้ปวดในกลุ่มอนุพันธ์ของฝิ่นเข้าช่องน้ำไขสันหลัง ผู้เข้าร่วมการวิจัยได้ถูกแบ่งออกเป็น 2 กลุ่มๆ ละ 17 คนโดยสุ่ม คือ 1) กลุ่มที่ได้รับถุงเจลให้ความเย็นประคบบริเวณแผลผ่าตัดเป็นเวลา 20 นาที อีกกลุ่มคือกลุ่มควบคุมไม่ได้รับถุงเจลให้ความเย็น บันทึกระดับความเจ็บปวดหลังผ่าตัดโดยใช้ภาพอนาล็อกมาตราส่วน (visual analog scale; VAS)โดยตัวผู้เข้าร่วมการวิจัยเองที่ 2 ชั่วโมงหลังคลอด (ก่อนได้รับถุงเจลให้ความเย็น), 6 ชั่วโมงหลังคลอด (4 ชั่วโมงหลังได้รับถุงเจลให้ความเย็น) และ 24 ชั่วโมงหลังคลอด รวมถึงบันทึกปริมาณยาแก้ปวดที่ต้องการเพิ่มเติม, การตกเลือดหลังคลอด, การติดเชื้อของแผลผ่าตัด, ความพึงพอใจ, ระยะเวลาในการนอนโรงพยาบาล และผลข้างเคียงจากการใช้ถุงเจลให้ความเย็น*

ผลการศึกษา: *ระดับความเจ็บปวดที่ 6 ชั่วโมงหลังคลอด ในกลุ่มที่ได้รับถุงเจลให้ความเย็นน้อยกว่ากลุ่มควลคุมอย่างมีนัยสำคัญ ค่าเฉลี่ยระดับความเจ็บปวด (mean pain score ± SD) 3.53 ± 2.12 และ 5.44 ± 1.56 ในกลุ่มควบคุม (p = 0.005), ในขณะที่ระดับความเจ็บปวดตั้งต้นที่ 2 ชั่วโมงและ 24 ชั่วโมงหลังคลอด ไม่แตกต่างกัน ความต้องการยาแก้ปวดเพิ่มเติม การตกเลือดหลังการผ่าตัดคลอด ระยะเวลานอนโรงพยาบาล การติดเชื้อของแผลผ่าตัดคลอดไม่มีความแตกต่างอย่างเป็นนัยสำคัญทางด้านสถิติ ส่วนความพึงพอใจอยู่ในระดับปานกลางถึงมากทั้งสองกลุ่มแต่ไม่มีความแตกต่างอย่างเป็นนัยสำคัญทางด้านสถิติ นอกจากนี้ยังไม่พบอาสาสมัครใดมีผลข้างเคียงจากการได้รับถุงเจลให้ความเย็น*

สรุป: *การใช้ถุงเจลให้ความเย็นเพื่อช่วยลดความเจ็บปวดหลังการผ่าตัดคลอดสามารถช่วยลดความเจ็บปวดจากการผ่าตัดคลอดได้อย่างมีประสิทธิภาพ ที่ระยะเวลา 6 ชั่วโมงหลังคลอด*

คำสำคัญ: *ถุงเจลให้ความเย็น, ความเจ็บปวดหลังผ่าตัด, การผ่าตัดคลอดบุตรทางหน้าท้อง*

Introduction

Effective postoperative pain control has been shown to relate to high patient satisfaction, rapid recovery, lower risk of deep vein thrombosis, heart and pulmonary complications and reduced costs of treatment[1].

In addition to conventional pharmacological postoperative pain management, a non-pharmacological approach has also been used in patients receiving operations. Among many modalities, cryotherapy has been increasingly used both as primary and adjunctive postoperative analgesia. It is believed that cryotherapy may reduce postoperative pain through decreasing the activation threshold of tissue nociceptors and the conduction velocity of pain nerve signals. Besides, this technique may help reduce pain through its effect on reduced cell metabolism and inflammation[2] and a decreased risk of surgical wound infection[3].

However, clinical benefits of cryotherapy on postoperative pain control remain uncertain. Although cryotherapy has reportedly been helpful as primary analgesia and adjunct analgesia in some surgical operations; for example, abdominal[4] and inguinal hernia surgeries[5] and emergency laparotomy[3]. The evidence of its benefits on pain control in obstetric and gynecologic operations is limited and available studies showed inconsistent results[6,7]. While the previous study showed that cryotherapy using cold gel pack could reduce postoperative pain in gynecologic surgeries under general anesthesia[6], other study suggested no benefits on pain control in Cesarean section[7]. In Cesarean delivery, neuraxial opioids were usually added during regional anesthesia (subarachnoid block) and adjunct analgesia may be needed for effective postoperative pain control. This study aimed to evaluate the efficacy of using cold gel pack as an adjunct analgesia in reducing postoperative pain in women undertaking Cesarean delivery under regional anesthesia (subarachnoid blockage) with neuraxial opioid at a referral tertiary hospital. We also examined the adverse effects and safety of cold gel pack as well as patient satisfaction.

Materials and Methods

Women aged 17-45 years old who underwent emergency or elective Cesarean delivery under regional anesthesia with neuraxial opioid from December 18th, 2019 to March 18th, 2020 at Sanpasitthiprasong hospital were invited to participate in this 2-arm parallel-group randomized control trial. The women who received parecoxib (Dynastat®), had a history of cold hypersensitivity, had any lesions at surgical wound, or developed severe complications during intra- and postpartum period, such as, cardiac arrest, eclampsia, and respiratory failure, were excluded from this study. This study was registered at http://www.thaiclinicaltrials.gov (TCTR20200205004) and was approved by the Sanpasitthiprasong Hospital Ethics Committee (Ref. no: 041/62C).

After giving written informed consent, baseline sociodemographic data, such as, age, occupation, education, income, types of health insurance, were recorded. Data on clinical and obstetric characteristics were obtained, and these included gravidity, parity, abortion, gestational age (GA), body mass index (BMI), mother's antenatal complications, obstetric complications, indication of operation, details of operation, type of skin incision, operative time, surgeons, and intraoperative blood loss.

After that, the participants were randomized into 2 groups: 1) receiving cold gel pack to cover surgical wound for 20 minutes at 2-hour after surgery in adjunct to standard pain control (intervention group), use only 1 cold gel pack. Nurses did not change cold gel pack during applying or 2) receiving standard pain control which was neuraxial opioids and additional analgesia such as paracetamol and pethidine (control group). Randomization numbers were generated using Microsoft Excel version 2010 and put in sealed opaque envelops.

At 2 hours postdelivery, the surgical wound of participants in the intervention group was covered by 5-plies-gauzed and waterproof-adhesive wrapped (Tegaderm® without pad) and cold gel pack which was wrapped by 2 mm-thick clothes. The cold gel

pack was frozen and stored at -10 C to 0 C for a minimum of 2 hours before using.

Primary outcomes were pain scores at 2 hours, 6 hours, and 24 hours post Cesarean delivery. Pain scores were assessed using visual analogue scale[8]. The participants put a mark on a 10 cm long straight line with the terms "no pain" at the left most and "the most unbearable pain" at the right most ends. Secondary outcomes included additional analgesia required, postpartum hemorrhage, surgical wound infection, length of hospital stays, patient's satisfaction, and adverse effects of cold gel pack.

Estimated total blood loss was computed based on recorded intraoperative blood loss and tampon used within 24 hours postpartum. Each tampon was weighed before and after using to estimate the volume of blood loss. Postpartum hemorrhage was defined as blood loss of at least 1,000 ml within 24 hours postdelivery. Surgical wound infection was defined as the presence of one or more symptoms/ signs of infections: pain or tenderness around the incision site, localized swelling, redness, or warmness, with or without pus draining within 7-10 days after procedures[9]. In this study, the surgical wound was opened in the third day to evaluate surgical wound infection before discharge. Length of hospital stays counted in days from admission until discharge. Patient's satisfaction was evaluated as being highly satisfied, moderate satisfied and dissatisfied at 24 hours after delivery.

Statistical analyses

From previous studies, there had researches about cryoanalgesia in obstetrics such as inflammation and pain in postpartum mothers[10], efficacy of cryoanalgesia in decreasing pain during second trimester genetic amniocentesis: a randomized trial[11]. The first research was different from our study due to different position of wound. Second research had less pain from our study therefore these 2 studies were difficult to compare.

Sample size was calculated to address the research question "whether cold gel pack as an adjunct was efficacious in postoperative pain control in Cesarean delivery." Based on results from a study by Nuangpho W, et al[6] which showed that cold gel pack reduced postoperative pain at 6 hours after benign gynecologic surgery, with a percentage of having reduced or mild postoperative pain being 75% and 0% in cold gel pack and control groups. Using the formula below, at 99% confidence level ($\alpha = 0.01$), 90% power ($\beta = 0.1$) and 20% missing data and loss of follow-up assumed, 17 participants were required in each group.

Statistical analysis was performed using SPSS version 25.0 (SPSS Inc., Chicago, IL, USA). Descriptive statistics: number (percentage), mean (± standard deviation (SD)), median (interquartile range (IQR)) were used to describe participant's characteristics. Continuous data was tested for their distribution using Komolokov-Smirnov test. Comparisons of these characteristics between the intervention and control groups were performed using chi-square test, student t-test, Mann-Whitney-U test for categorical, normally and non-normally distributed continuous variables, respectively. An intention-to-treat analysis was used. Pain scores as primary outcome were compared between the two treatment groups using the student t-test. Adverse events and complications were compared between the two groups using chi-square test. A p value of < 0.05 was considered statistically significant.

Results

Fig. 1. shows flow of participant recruitment, randomization, application of intervention and outcome ascertainment in this 2-arm parallel-group randomized control trial. A total of 37 participants were presented at Sanpasittiprasong Hospital, Department of Obstetrics and Gynecology during the study period. Two cases who refused to participate in this study, and additional one case who did not received neuraxial opioids during her regional anesthesia were excluded from this study, leaving a final study sample of 34 women, 17 in each group. There was no lost to follow-up in both groups.

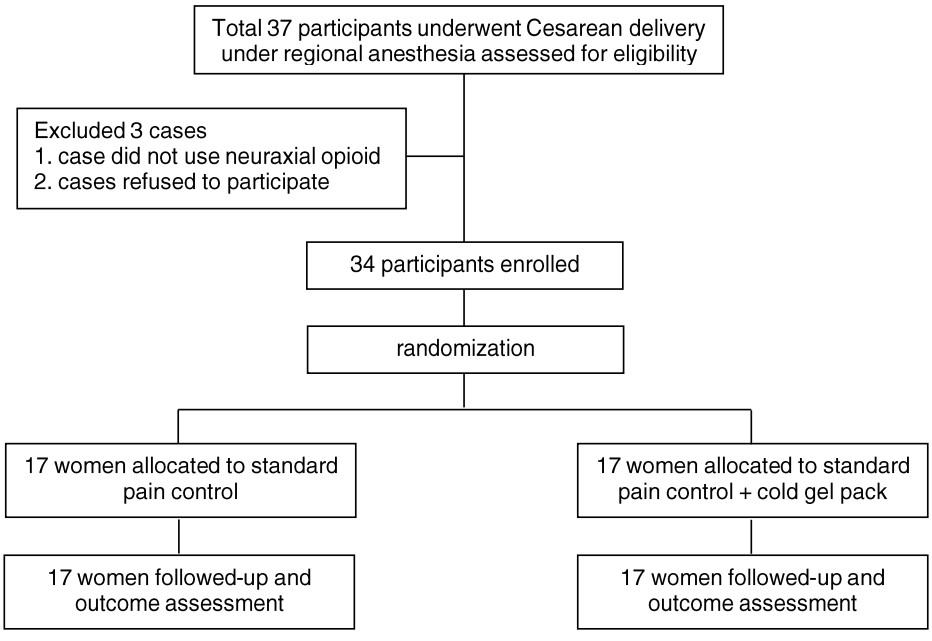

Fig. 1. Flow of recruitment, randomization, intervention and outcome ascertainment in this 2-arm parallel-group randomized control trial.

Table 1 shows sociodemographic, clinical and obstetric characteristics of study participants, total and by treatment groups. The median (IQR) age of study participants was 28.0 (26.0 - 32.0) years. Almost half of all participants were housewives. Two-thirds reported secondary school as the highest education and had universal coverage health insurance. Median gravidity and gestational age were 2.0 (IQR 1.0 - 3.0) and 39.0 (IQR 37.0 - 39.3) weeks, respectively. Approximately 56% and 41% of participants had cephalopelvic disproportion and previous cesarean section as an indication for Cesarean delivery. Most participants had low midline skin incision. Four-fifths of the Cesarean sections were performed by doctors in training and median operative time was 40.0 (IQR 35.8 - 49.0) minutes. Concerning intraoperative analgesia, median heavy marcaine of 1.95 ml and spinal morphine of 0.18 mg were used. Median intraoperative blood loss was 500 ml. Approximately 21% and 70% of participants had at least one of maternal complications and obstetric complications. The only characteristic found different between the two groups was indication for Cesarean section, where the intervention group had a higher proportion of cephalopelvic disproportion than the control group. All of the remaining sociodemographic, clinical and obstetric characteristics were comparable between those in the intervention and control groups.

Pain scores assessed at 2, 6 and 24 hours postdelivery in the intervention and control groups are presented in Table 2. The initial pain scores at 2 hours postdelivery before applying cold gel pack were comparable between the two treatment groups. After applying cold gel pack, difference in pain scores between treatment groups was observed, with significantly lower pain scores at 6 hours after delivery in the intervention than control groups ($p = 0.005$). There was no statistically significant difference in pain score evaluated at 24 hours postdelivery. Reduce/mild pain was no statistically significant difference evaluated at 2, 6 and 24 hours postdelivery.

Table 1. Baseline characteristics of participants.

	Total (n=34)	Intervention (n=17)	Control (n=17)	p value
Age (years)	28.0 (26.0, 32.0)	28.0 (26.0, 32.0)	27.0 (25.0, 30.0)	0.322
Occupation				0.424
Business	2 (5.9%)	1 (5.9%)	1 (5.9%)	
Housewife	15 (44.1%)	8 (47.1%)	7 (41.2%)	
Teacher	2 (5.9%)	2 (11.8%)	0 (0%)	
Employee	10 (29.4%)	5 (29.4%)	5 (29.4%)	
Farmer	5 (14.7%)	1 (5.9%)	4 (23.5%)	
Education				0.791
Primary school	2 (5.9%)	1 (5.9%)	1 (5.9%)	
Secondary school	23 (67.6%)	11 (64.7%)	12 (70.6%)	
Vocational school	3 (8.8%)	1 (5.9%)	2 (11.8%)	
Bachelor's degree	6 (17.6%)	4 (23.50)	2 (11.8%)	
Income (baht)				0.486
Less than 10,000	23 (67.6%)	12 (70.6%)	11 (64.7%)	
10,000 – 20,000	10 (29.4%)	4 (23.5%)	6 (35.3%)	
More than 20,000	1 (2.9%)	1 (5.9%)	0 (0%)	
Insurance				0.375
Universal coverage	22 (64.7%)	11 (64.7%)	11 (64.7%)	
Cash	1 (2.9%)	0 (0%)	1 (5.9%)	
Government welfare	2 (5.9%)	2 (11.8%)	0 (0%)	
Social worker welfare	9 (26.5%)	4 (23.5%)	5 (29.4%)	
Body mass index (kg/m2)	28.9 (24.9, 33.4)	31.2 (25.9, 34.5)	27.2 (24.7, 31.0)	0.493
Gravidity	2 (1.0, 3.0)	2 (1.0, 2.0)	2 (1.5, 3.0)	0.143
Parity	1 (0, 1.0)	0 (0,1.00)	1 (0.50,1.00)	1.000
Abortion	0 (0, 1.0)	0 (0,0)	0 (0,1.00)	0.120
Gestational age (weeks)	39.0 (37.0, 39.3)	39.0 (38.0, 40.0)	38.0 (36.0, 39.0)	0.686
Indication				0.046
Cephalopelvic disproportion	19 (55.9%)	13 (76.5%)	6 (35.3%)	
Previous Cesarean section	14 (41.2%)	4 (23.5%)	10 (58.8%)	
Unfavorable cervix	1 (2.9%)	0 (0%)	1 (5.9%)	
Operation				0.078
Cesarean section	21 (61.8%)	13 (76.5%)	8 (47.1%)	
Cesarean section with tubal resection	13 (38.2%)	4 (23.5%)	9 (52.9%)	
Skin incision				0.473
Low midline	22 (64.7%)	10 (58.8%)	12 (70.6%)	
Pfannenstiel	12 (35.3%)	7 (41.2%)	5 (29.4%)	
Operative time (min.)	40.0 (35.8, 49.0)	40.0 (35.5, 48.5)	40.0 (36.0, 51.5)	0.919
Heavy Marcaine (ml.)	1.95 (1.80, 2.00)	1.95 (1.75, 2.00)	1.95 (1.80, 2.00)	0.731
Spinal morphine (mg.)	0.18 (0.10, 0.20)	0.20 (0.15, 0.20)	0.10 (0.10, 0.20)	0.170
Surgeon				0.072
Staff	6 (17.6%)	5 (29.4%)	1(5.9%)	
Resident	28 (82.4%)	12 (70.6%)	16(94.1%)	
Intraoperative blood loss (ml.)	500 (500.0, 500.0)	500 (500.0, 500.0)	500 (500.0, 500.0)	1.000
Composite maternal complicationsa	7 (20.6%)	4 (23.5%)	3 (17.6%)	0.671
Composite obstetric complicationsb	24 (70.6%)	11 (64.7%)	13 (76.5%)	0.452

Data are presented as number (percentage) or median (interquartile range).

[a] composite maternal complications defined as the presence of one or more of the following complications: urinary tract infection, asthma, cerebrovascular sequelae, upper respiratory tract infection, diarrhea, chronic renal failure, sepsis, anemia

[b] composite obstetric complications defined as the presence of one or more of the following obstetric complications: premature ruptured of membrane, preterm labor, fetal growth restriction, elderly gravidarum, gestational diabetes mellitus, twin, pregnancy induced hypertension, obesity, teenage pregnancy

Table 2. Comparison of pain score between intervention and control groups at 2 hours (before intervention), 6 hours (4 hours after intervention) and 24 hours postdelivery.

Time after cesarean delivery	Intervention (n=17)	Control (n=17)	p value
Pain score			0.424
2 hours (before use cold gel pack)	2.67±2.20	4.19 ± 2.50	0.083
6 hours (after delivery)	3.53 ± 2.12	5.44 ± 1.56	0.005
24 hours (after delivery)	4.82± 1.99	4.57 ± 2.11	0.200
Reduce/mild paina	1 (5.9%)	4 (23.5%)	
2 hours (before use cold gel pack)	7 (41.2%)	10 (58.8%)	0.303
6 hours (after delivery)	8 (47.1%)	4 (23.5%)	0.151
24 hours (after delivery)	3 (17.6%)	6 (35.3%)	0.244

Data are presented as mean ± standard deviation or number (percentage).

[a] reduce/mild pain defined as pain score VAS < 4

Concerning postoperative outcomes, both the intervention and control groups required a similar amount of additional analgesia (Table 3). There was no statistically significant difference between the two treatment groups in amount of blood loss in 24 hours, postpartum hemorrhage, blood transfusion, length of hospital stays and surgical wound infection. Patient satisfaction was not different between the two groups. No adverse event of the cold gel pack was reported.

Table 3. Comparison between treatment groups in postoperative outcomes.

	Total (n=34)	Intervention (n=17)	Control (n=17)	p value
Additional analgesia				
Paracetamol 1 dose	9 (26.5%)	4 (23.5%)	5 (29.4%)	0.687
Pethidine 1 dose	3 (8.8%)	0 (0%)	3 (17.6%)	0.070
Infected surgical wound at day 3	1 (2.9%)	0 (0%)	1 (5.9%)	0.310
Infected surgical wound at day 10	1 (2.9%)	0 (0%)	1 (5.9%)	0.310
24 hours blood loss (ml)	622.0 (586.5,660.0)	612.0 (577.0,652.0)	631.0 (599.5,678.5)	0.150
Postpartum hemorrhage	0 (0%)	0 (0%)	1 (5.9%)	0.310
Satisfaction				0.730
Dissatisfied	0 (0%)	0 (0%)	0(0%)	
Neutral	15 (44.1%)	7 (41.2%)	8 (47.1%)	
Satisfied	19 (55.9%)	10(58.8%)	9(52.9%)	
Length of hospital stay (days)	2.5 (2.0,3.0)	2(2.0,3.0)	3(2.0,3.0)	0.786

Data are presented as number (percentage) or median (interquartile range).

Table 4 shows neonatal outcomes in the intervention and control groups. The birthweight of neonates was significantly higher in the intervention than control groups (mean ± SD weight 3,456.18 ± 565.8 and 2,633.24 ± 842.57 grams, respectively, p = 0.002). There was no difference between the two groups in Apgar scores at 1, 5 and 10 minutes, intubation and other neonatal morbidities. Some neonatal complications were reported and these included neonatal jaundice, polycythemia, hypoglycemia, neonatal anemia, birth asphyxia, urinary tract infection and respiratory complications as well as serious complications, namely acute renal failure, respiratory distress syndrome, neonatal sepsis, and intraventricular hemorrhage. However, there was no difference in the occurrence of these neonatal complications between the two treatment groups.

Table 4. Comparison between treatment groups in neonatal outcomes.

	Total (n=34)	Intervention (n=17)	Control (n=17)	p value
Birthweight (gram)	3044.7 ± 820.9	3456.2 ± 565.8	2633.2 ± 842.6	0.002
Apgar at				
1 minute	9 (9.0, 9.0)	9 (9.0, 9.0)	9 (8.0, 9.0)	0.150
5 minutes	10 (10.0, 10.0)	10(10.0, 10.0)	10(9.8, 10.0)	0.245
10 minutes	10 (10.0, 10.0)	10(10.0, 10.0)	10(10.0,10.0)	0.786
Intubation	2(5.90%)	0(0%)	2(11.8%)	0.145
Composite neonatal complicationsa	13(38.2%)	6(35.3%)	7(41.2%)	0.724
Composite neonatal respiratory complicationsb	18(52.9%)	8(47.1%)	10(58.8%)	0.730
Composite neonatal serious complicationsc	3(8.8%)	0(0%)	3(17.6%)	0.070

Data are presented as number (percentage), mean ± standard deviation, or median (interquartile range).

[a] Composite neonatal complications defined as the presence of one or more of the following neonatal complications: neonatal jaundice, polycythemia, hypoglycemia, neonatal anemia, birth asphyxia, urinary tract in+fection

[b] Composite neonatal respiratory complications defined as the presence of one or more of the following complications: transient tachypnea of newborn, pneumonia, respiratory distress syndrome, nasal block, persistent pulmonary hypertension, atelectasis, delayed adaptation, bronchopulmonary dysplasia, meconium aspiration syndrome.

[c] Composite neonatal serious complications defined as the presence of one or more of the following neonatal complications: acute renal failure, respiratory distress syndrome, neonatal sepsis, intraventricular hemorrhage.

Discussion

In this 2-arm randomized control trial, cold gel pack significantly reduced postoperative pain at 6 hours after Cesarean delivery but such the benefit did not maintain up to 24 hours postdelivery. It should use cold gel pack for longer period; however, it must observe complication such as back pain, frostbite. There was no significant of additional analgesia required, postpartum hemorrhage, length of hospital stays, satisfaction, surgical wound infection and neonatal complications between the two groups.

Among many modalities of postoperative analgesia using for abdominal surgery, especially for Cesarean section, subarachnoid block with neuraxial opioid is preferred. Although this analgesia used, there were some patients suffered from postoperative pain and required additional analgesic drugs[12]. This study demonstrated the efficacy of cold gel pack as an adjunctive analgesia for post Cesarean delivery which significantly reduced pain score at 4 hours after applying. Cryotherapy induces effects both locally and at the level of the spinal cord via neurologic and vascular mechanisms. Topical cold treatment decreases the temperature of the skin and underlying tissues to a depth of 2 to 4 cm, decreasing the activation threshold of tissue nociceptors and the conduction velocity of pain nerve signals[2]. This effect might not last for long that was proved by losing its effect at 24 hours after delivery. This may be explained that the pain after Cesarean delivery also caused by the visceral pain from uterine contraction which could not be affected by this topical therapy. The efficacy of cold gel pack in our study was similar to recent studies in gynecologic surgery[6,13,14]. For further analgesia beyond 24 hours post-surgery, the additional applying might be needed[4].

Our study was different from Kılıc E, et al[3] which reported no difference in pain score between treatment group with therapeutic hypothermia for pain control in urgent abdominal surgery. This may be explained by timeframe evaluation of pain score and the general anesthesia in emergency laparotomy cases while our study evaluated pain score at specific point of time after surgery in Cesarean delivery participants under spinal anesthesia with neuraxial opioid.

Subarachnoid block with spinal morphine in total abdominal hysterectomy lasted for 90 minutes. Median pain score of 4-5 and 27-30% requirement of additional analgesia observed in previous study[15]. Whereas in setting of Cesarean section in our study, with similar pain score and proportion additional analgesic requirement, cold gel pack could exert more effects with less pain score of 3-4 and 23.5% additional paracetamol usage. This may because of less devastating tissue injury in Cesarean section than total abdominal

hysterectomy.

The decreased blood flow effect of cold gel pack[16] might affect the amount of blood loss postpartum. This study clearly showed that cold gel pack did not affect either postpartum hemorrhage or amount of blood loss in 24 hours post Cesarean delivery which correlate with previous study[17]. Regarding the effect of decreased inflammation[2], this study also showed that cold gel pack did not increased risk of surgical wound infection which consistent with previous study[3]. The length of hospital stays in our study was not significantly different between two groups because there was no serious postpartum complication which prolonged hospital stays in both groups.

Although the cold gel pack cooling efficiency was reported around 31 minutes[18], but in our study proved that its effect still remains at 4 hours after applying. This may be explained by many mechanisms such as decreased muscle spasm, decreased blood supply, and reduced inflammation[2]. According to safety data, application of cold gel pack for 20 minutes caused least cooling compared to other modalities[18] which may cause frost bite[19]. In this study, there was no complication from cold gel pack found. Since cold gel pack was applied after delivery, there was no adverse neonatal effect.

This study was the well-designed randomized controlled trial proved efficacy of cold pack gel as an adjunctive analgesia after Cesarean delivery with no adverse effect and insignificant maternal complications. Cold gel pack may be routine use in adjunctive reducing postoperative pain after Cesarean delivery. However, there was limitation of double blinding which was impossible due to nature of cold gel pack. There was more proportion of Cesarean delivery due to cephalopelvic proportion in intervention group which resulted in significant higher neonatal birthweight. This might be another factor affecting pain score evaluated postpartum.

Conclusion

Cold gel pack was efficacious in adjunctive reducing postoperative pain after Cesarean delivery under spinal anesthesia with neuraxial opioid at 6 hours without significant complications.

Potential conflicts of interest

The authors declare no conflicts of interest.

References

1. Ramsay MAE. Acute postoperative pain management. Proc Bayl Univ Med Cent 2000;13:244-7.
2. Nadler SF, Weingand K, Kruse RJ. The physiologic basis and clinical applications of cryotherapy and thermotherapy for the pain practitioner. Pain Physician 2004;7:395-9.
3. Kılıc E, Ugur M. Effect of therapeutic hypothermia on superficial surgical site infection and postoperative pain in urgent abdominal surgery. Ulus Travma Acil Cerrahi Derg 2018;24:417-22.
4. Watkins AA, Johnson TV, Shrewsberry AB, Nourparvar P, Madni T, Watkins CJ, et al. Ice packs reduce postoperative midline incision pain and narcotic use: a randomized controlled trial. J Am Coll Surg 2014;219: 511-7.
5. Koc M, Tez M, Yoldas O, Dizen H, Gocman E. Cooling for the reduction of postoperative pain: prospective randomized study. Hernia 2006;10:184-6.
6. Nuangpho W, Srinil S, Tangsiriwatthana T, Sripipattanakul M. Gel pack reduced postoperative pain in benign gynecologic surgery: a randomized controlled trial. Thai J Obstet Gynaecol 2018;26:52-8.
7. Amin-Hanjani S, Corcoran J, Chatwani A. Cold therapy in the management of postoperative cesarean section pain. Am J Obstet Gynecol 1992;167:108-9.
8. Heller GZ, Manuguerra M, Chow R. How to analyze the visual analogue scale: Myths, truths, and clinical relevance. Scand J Pain 2016;13:67-75.
9. CDC. Surgical site infection (SSI) Event. Procedure-associated module [Internet]. 2020 [cited 2020 Sep 20];9-1-36. available from: http://www.cdc.gov/nhsn/pdfs/pscmanual/9pscssicurrent.pdf
10. Janmanee T, Yusamran C, Ratinthorm, Phahuwatanakorn W. Effects of cooling and heat application on perineal inflammation and pain in postpartum. J Nurs Sci 2014; 32:25-34.
11. Hanprasertpong T, Kor-anantakul O, Prasartwanakit V, Leetanaporn R, Suntharasaj T, Suwanrath C. Efficacy of cryoanalgesia in decreasing pain during second trimester genetic amniocentesis: a randomized trial. Arch Gynecol Obstet 2012;286:563-6.
12. Kanazi GE, Aouad MT, Abdallah FW, Khatib MI, Adham AMBF, Harfoush DW, et al. The analgesic efficacy of subarachnoid morphine in comparison with ultrasound-

guided transversus abdominis plane block after cesarean delivery: a randomized controlled trial. Anesth Analg 2010;111: 475-81.
13. Ravindhran B, Rajan S, Balachandran G, Mohan LN. Do ice packs reduce postoperative midline incision pain, NSAIDS or narcotic use? World J Surg 2009;43:2651-7.
14. Chumkam A, Pongrojpaw D, Chanthasenanont A, Pattaraarchachai J, Bhamarapravatana K, Suwannarurk K. Cryotherapy reduced postoperative pain in gynecologic surgery: a randomized controlled trial. Pain Res Treat 2019;2019:1-6.
15. Campos GO, Martins MJ, Jesus GN, Rios PR, Lessa CN, Fernandes JCM, et al. Palonosetron versus ondansetron for prevention of nausea and vomiting after total abdominal hysterectomy under spinal anesthesia with intrathecal morphine: a double-blind, randomized controlled trial. BMC Anesthesiology 2019;19:159.
16. Weston M, Taber C, Casagranda L, Cornwall M. Changes in local blood volume during cold gel pack application to traumatized ankles. JOSPT 1994;19:197-9.
17. Masuzawa Y, Kataoka Y, Nakamura S, Yaju Y. Cooling the lower abdomen to reduce postpartum blood loss: A randomized controlled trial. PLoS ONE 2017;12: e0186365.
18. Kennet J, Hardaker N, Hobbs S, Selfe J. Cooling Efficiency of 4 Common Cryotherapeutic Agents. J Athl Train 2007;42:343-8.
19. Rivlin M, King M, Kruse R, Ilyas AM. Frostbite in an Adolescent Football Player: A Case Report. J Athl Train 2014;49:97-101.

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GYNAECOLOGY

Laparoscopic Radical Hysterectomy for Early-stage Cervical Cancer: Experiences from Rajavithi Hospital

Aranya Yantapant, M.D.*,
Chumnan Kietpeerakool, M.D.**

** Department of Obstetrics and Gynecology, Rajavithi Hospital, College of Medicine, Rangsit University, Bangkok, Thailand*
*** Department of Obstetrics and Gynecology, Faculty of Medicine, Khon Kaen University, Thailand*

ABSTRACT

Objectives: To assess the survival outcomes of women with cervical cancer who had been treated with laparoscopic radical hysterectomy (LRH) at a large referral center in Thailand.

Materials and Methods: Records of women undergoing LRH between January 2010 and December 2018 were reviewed.

Results: Of 67 patients, the median age was 49 years. Fifty-six patients (83.6%) were diagnosed with stage IB cervical cancer. Forty-two (62.7%) patients had squamous cell carcinoma. Twenty-five (37.3%) patients received adjuvant treatment following LRH. With a median follow-up time of 32.6 months, eight (11.9%) patients experienced recurrent disease including pelvic recurrence (six patients) and combined pelvic and distant recurrences (two patients). Their 5-year disease-free (DFS) and overall survivals (OS) were 75.4% and 76.8%, respectively. Patients with squamous cell carcinoma had longer DFS than those with other histological types ($p = 0.028$).

Conclusion: The 5-year DFS and OS of patients undergoing LRH in this study were 75.4% and 76.8%, respectively. Patients with squamous cell carcinoma had longer survival than those with other histological types.

Keywords: cervical cancer, radical hysterectomy, laparoscopy, laparotomy, minimally invasive surgical procedures.

Correspondence to: *Chumnan Kietpeerakool, M.D., Department of Obstetrics and Gynecology, Faculty of Medicine, Khon Kaen University, Khon Kaen 40000, Thailand. E-mail: kiet_ji@hotmail.com*

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การตัดมดลูกออกแบบกว้างผ่านกล้องสำหรับมะเร็งปากมดลูกระยะต้น: ประสบการณ์จากโรงพยาบาลราชวิถี

อรัญญา ยันตพันธ์, ชำนาญ เกียรติพีรกุล

บทคัดย่อ

วัตถุประสงค์: *เพื่อประเมินผลการรักษาในสตรีที่พบมะเร็งปากมดลูกระยะต้นที่ได้รับการตัดมดลูกออกแบบกว้างผ่านกล้องที่โรงพยาบาลที่เป็นศูนย์รับการส่งตัวขนาดใหญ่ในประเทศไทย*

วัสดุและวิธีการ: *ทบทวนบันทึกเวชระเบียนของสตรีที่ได้รับการรักษาด้วยการตัดมดลูกออกแบบกว้างผ่านกล้องในช่วงเดือนมกราคม พ.ศ. 2553 ถึง เดือนธันวาคม พ.ศ. 2561*

ผลการศึกษา: *จากจำนวนผู้ป่วยทั้งสิ้น 67 ราย มีค่ามัธยฐานของอายุเท่ากับ 49 ปี ผู้ป่วย 56 ราย (ร้อยละ 83.6) ได้รับการวินิจฉัยว่าเป็นมะเร็งปากมดลูกระยะ IB ผู้ป่วย 42 ราย (ร้อยละ 62.7) พบมะเร็งชนิดสเควมัสเซลล์ ผู้ป่วย 25 ราย (ร้อยละ 37.3) ได้รับการรักษาเสริมภายหลังการผ่าตัด จากค่ามัธยฐานของระยะเวลาในการติดตามการรักษาที่เวลา 32.6 เดือน ผู้ป่วย 8 ราย เกิดการกลับเป็นซ้ำของโรค โดยเป็นการกลับเป็นซ้ำในอุ้งเชิงกรานจำนวน 6 ราย และการกลับเป็นซ้ำที่พบทั้งในอุ้งเชิงกรานและการกลับเป็นซ้ำในตำแหน่งไกลจำนวน 2 ราย การรอดชีวิตปลอดโรคและรอดชีวิตโดยรวมที่ระยะเวลา 5 ปี เท่ากับร้อยละ 75.4 และร้อยละ 76.8 ตามลำดับ ผู้ป่วยที่มีมะเร็งชนิดสเควมัสเซลล์จะมีการรอดชีวิตปลอดโรคยาวนานกว่าผู้ป่วยที่มีมะเร็งชนิดอื่น (p = 0.028)*

สรุป: *การรอดชีวิตปลอดโรคและรอดชีวิตโดยรวมที่ระยะเวลา 5 ปี ของผู้ป่วยมะเร็งปากมดลูกที่ได้รับการตัดมดลูกแบบกว้างผ่านกล้องในการศึกษานี้เท่ากับร้อยละ 75.4 และ ร้อยละ 76.8 ตามลำดับ ผู้ป่วยที่มีมะเร็งชนิดสเควมัสเซลล์จะมีการรอดชีวิตยาวนานกว่าผู้ป่วยที่มีมะเร็งชนิดอื่น*

คำสำคัญ: *มะเร็งปากมดลูก, การตัดมดลูกออก. การผ่าตัดผ่านกล้อง, การผ่าตัดเปิดหน้าท้อง, การผ่าตัดที่มีการลุกล้ำน้อย*

Introduction

Cervical cancer was responsible for an estimated 570,000 cases and 311,000 deaths worldwide in 2018[1]. This disease is prevalent in less developed countries with age-standardized incidence rates of 18.2 and 10.4 per 100,000 females in low/medium human development index (HDI) and high/very-high HDI countries, respectively[1]. Most cervical cancer deaths occur in low/medium HDI countries[1,2].

Treatment for cervical cancer depends on the disease stage[2-4]. Radical hysterectomy with bilateral pelvic lymphadenectomy is the standard surgical treatment for stage Ia2-IIa cervical cancer when preservation of fertility is not required or feasible[2-4]. Concurrent chemoradiation is also accepted as a standard treatment option for women with early-stage cervical cancer[5]. Radical hysterectomy and concurrent chemoradiation are equivalent treatments for early-stage cervical cancer[5]. Decisions regarding treatment therefore depend on individual patient characteristics and preferences and consideration of the perioperative risks with the longer-term risks of radiation[2].

Radical hysterectomy can be performed via laparotomy (open surgery) and minimally invasive surgery (MIS). A randomized study by Ramirez, et al[6] and the Surveillance, Epidemiology, and End Results data analysis by Melamed, et al[7] consistently observed that the minimally invasive surgical approach for radical hysterectomy for cervical cancer was associated with increased rates of recurrence and death compared with open surgery. These findings were reaffirmed in a population-based cohort study undertaken in the United States that noted that minimally invasive radical hysterectomy was associated with a 2-fold higher rate of death and recurrence compared with open radical hysterectomy in patients with stage IB disease while accounting for mechanistic factors including patient characteristics and surgeon volume[8]. Nevertheless, the difference in survival between MIS and an open surgical approach in the subgroup of women with tumors ≤ 2 cm seems to be comparable[6].

Because the reasons leading to poorer oncological outcomes for women undergoing radical hysterectomy for cervical cancer treated by MIS compared with open radical hysterectomy remain debatable, careful counseling based on the available data to determine the appropriate surgical approach for an individual patient is important. Therefore, information regarding the factors affecting treatment outcome among patients undergoing minimally invasive radical hysterectomy is required to identify a subset of patients who remain suitable for this procedure. This study was conducted to evaluate the outcomes of women with cervical cancer who were treated with laparoscopic radical hysterectomy (LRH) at Rajavithi Hospital, a large referral center in Thailand. Factors associated with the outcomes of this surgical approach were also assessed.

Materials and Methods

After receiving approval from the Research Ethics Committee, the medical records of women with cervical cancer undergoing LRH at Rajavithi Hospital between January 2010 and December 2018 were reviewed. Abstracted data included patients' baseline characteristics, stage of the disease, tumor size, cell types, and survival outcomes.

The cervical cancer was clinically staged according to the International Federation of Gynecology and Obstetrics staging classification[9]. All operations were performed by gynecologic oncologists with in-training fellows as assistants. All patients underwent complete bilateral pelvic lymphadenectomy. The tumor diameter was clinically measured. The deep cervical stromal invasion was defined as invasion of cancer to the outer one-third of the cervical stroma.

Adjuvant treatment was considered if at least one of the following major risk factors for disease recurrence were noted: vaginal margin involvement, parametrial extension, and lymph node metastasis. Adjuvant chemotherapy may be considered in women with neuroendocrine carcinoma of the cervix although there were no major pathological risk factors noted.

Disease-free survival (DFS) was defined as the time between the date of the operation and the date of diagnosis of recurrence. Overall survival (OS) was defined as the time frame between the date of the operation and the date of death from any cause.

Statistical analysis was conducted via STATA (Stata Corporation, College Station, Texas). The demographic characteristics of the patients were summarized as number (percentage) or mean ± standard deviation (SD) as appropriate. DFS and OS were estimated using the Kaplan-Meier method and differences in survival were compared using the log-rank test.

Results

During the study period, records of 71 women undergoing LRH as the primary treatment for early-stage cervical cancer were available for review. Four cases were excluded because of conversion to open radical hysterectomy due to bladder injury (1), vascular injury (1), and technical difficulty (2), which left 67 records for analysis.

Baseline characteristics and perioperative outcomes

Table 1 displays patients' baseline characteristics and perioperative outcomes. The median age of the patients was 49 years (interquartile range 41, 56 years). Four patients (6.0%) were nulliparous. Fifty-six patients (83.6%) were diagnosed with stage IB cervical cancer. Forty-two (62.7%) patients had squamous cell carcinoma. Urinary tract injury was noted in two (3.0%) patients.

Table 1. Population characteristics.

Characteristic	N = 67
Parity status	
Nulliparous	4 (6.0%)
Multiparous	63 (94.0%)
Presence of underlying medical comorbidity[1]	33 (49.3%)
History of a previous cesarean section	2 (3.0%)
FIGO stage	
IA	11 (16.4%)
IB	56 (83.6%)
Histology	
Squamous cell carcinoma	42 (62.7%)
Adenocarcinoma	16 (23.9%)
Adenosquamous carcinoma	2 (3.0%)
Others	7 (10.5%)
Operative time (hours), median (IQR)	4.10 (3.40-4.55)
Estimated blood loss (mL), median (IQR)	200 (100-300)
Perioperative complications	
None	61 (91.0%)
Urinary tract infection	3 (4.5%)
Ureteric injury	2 (3.0%)
Urinary retention	1 (1.5%)

IQR: interquartile range; FIGO: International Federation of Gynecology and Obstetrics

[1] including hypertension, diabetes, thyroid function disorder, and dyslipidemia.

Histopathological outcomes

Of 67 LRH specimens, nine (13.4%) and twelve (17.9%) had parametrial invasion and vaginal margin involvement, respectively. Lymphovascular space invasion and deep cervical stromal invasion were noted in 31 (46.3%) and 45 (67.2%) of LRH specimens, respectively. The median number of pelvic lymph nodes yielded per case was 13 (interquartile range 10, 17). Pelvic lymph node metastasis was observed in five (7.5%) patients (Table 2).

Oncological outcomes

Twenty-five (37.3%) patients received adjuvant treatment following LRH. With a median follow-up time of 32.6 months (interquartile range 19.8, 44.8), eight (11.9%) patients experienced recurrent disease including pelvic recurrence (six patients) and combined pelvic and distant recurrences (two patients) (Table 2). The 5-year DFS and OS of the entire cohort were 75.4% and 76.8%, respectively.

Table 2. Histopathological and oncological outcomes.

Oncological outcomes	N = 67
Pelvic lymph node metastasis	5 (7.5%)
Parametrial metastasis	9 (13.4%)
Lymphovascular space invasion	31 (46.3%)
Vaginal margin involvement	12 (17.9%)
Outer one-third of cervical stromal invasion	45 (67.2%)
Type of adjuvant treatment received	
Pelvic radiation	14 (20.9%)
Concurrent chemoradiation	7 (10.5%)
Chemotherapy	4 (6.0%)
None	42 (62.7%)
Recent status	
Alive without disease	59 (88.1%)
Alive with disease recurrence	4 (6.0%)
Death	4 (6.0%)
Recurrence	
None	59 (88.1%)
Pelvic recurrence	6 (9.0%)
Distant recurrence	0 (0.0%)
Combined pelvic/distant recurrences	2 (3.0%)

Fig. 1 and 2 show the DFS stratified by the histological type and size of the tumor. Patients with squamous cell carcinoma had longer DFS than those with other histological types ($p = 0.028$). There was no statistically significant difference in terms of DFS between patients with tumor size ≤ 2 cm and those who had larger tumors ($p = 0.573$). Patients with squamous cell carcinoma tended to have longer OS than those with other histological types ($p = 0.069$) (Fig. 3). No statistically significant difference in OS was noted when patients were stratified by tumor size ($p = 0.658$) (Fig. 4).

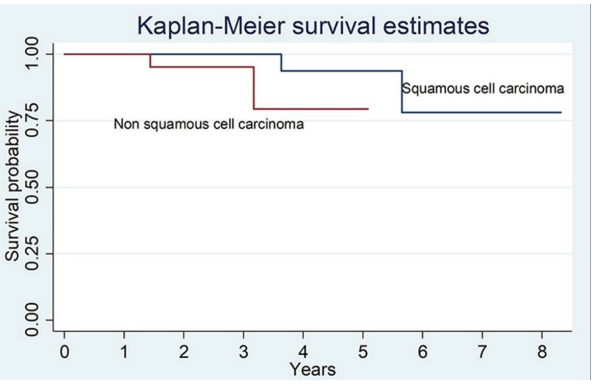

Fig. 1. Disease-free survival stratified by tumor histological type.

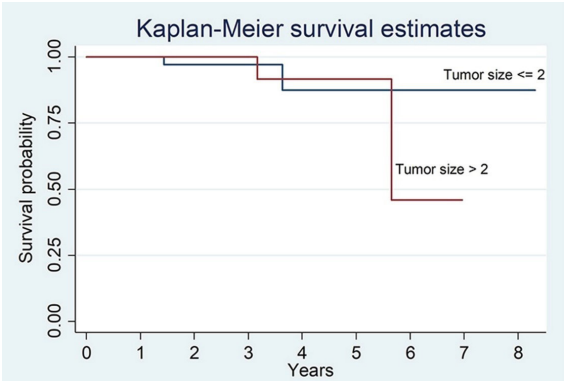

Fig. 2. Disease-free survival stratified by tumor size.

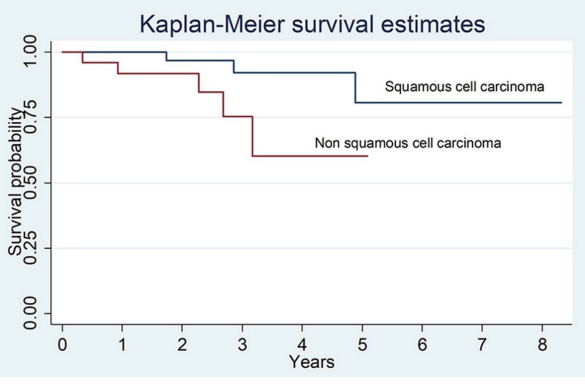

Fig. 3. Overall survival stratified by tumor histological type.

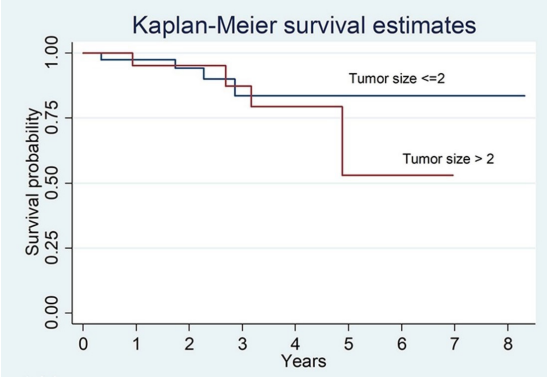

Fig. 4. Overall survival stratified by tumor size.

Discussion

In this study, we reported the survival and prognostic factors of patients with early-stage cervical cancer treated by LRH. Patients' 5-year DFS and OS were 75.4% and 76.8%, respectively. The factor potentially associated with poorer outcome was tumor histological type. To our knowledge, this study is the first to report on LRH in Thailand, regarding survival outcomes.

In this study, the survival of patients with cervical cancer stage IA-IB who were treated with LRH was considerably lower than that of patients who underwent open radical hysterectomy in previously reported findings[10-12]. The 5-year survival rates of women undergoing open radical hysterectomy for stage Ia2 to IIa cervical cancer are over 80%[10-12]. Mahawerawat et al[11] found that the 5-year DFS and OS among women with cervical cancer stage IA2 who were treated with open radical hysterectomy were 97.4% and 97.4%, respectively. Srisomboon, et al[12] noted that the 5-year DFS of 680 patients with cervical cancer stage IB treated with open radical hysterectomy ranged from 83% to 98% depending on the tumor size. The significant inferiority of the minimally invasive approach for radical hysterectomy has been demonstrated in a recent prospective randomized trial and some large cohort studies[6-8].

Determination of the factors affecting treatment outcome among patients undergoing minimally invasive radical hysterectomy may be helpful for

identifying a subset of patients for whom minimally invasive radical hysterectomy remains safe. Ramirez, et al[6] showed a significantly better survival using open surgery for cervical cancer for large tumors (> 2 cm) compared with minimally invasive radical hysterectomy. In a subgroup analysis of data from the Surveillance, Epidemiology, and End Results study, the impact of surgical approach routes for radical hysterectomy on survival of patients with small tumors was not apparent. For patients with tumors smaller than 2 cm in the greatest dimension, the likelihood of death following minimally invasive radical hysterectomy was comparable with open radical hysterectomy (hazard ratio 1.46, 95% confidence interval 0.70-3.02)[7]. In our study, patients with tumors larger than 2 cm who underwent LRH tended to have shorter survival than those with smaller tumors, although the difference was not statistically significant (Fig. 2 and 4). Additionally, patients with squamous cell carcinoma had longer survival than those with other histological types. The oncological safety following minimally invasive radical hysterectomy in women with small cervical tumors and those who had squamous cell carcinoma histology should be confirmed in a large-scale study.

The dissemination of cancer cells into the peritoneal cavity has been proposed to be a potential reason for the inferior oncologic outcomes after minimally invasive radical hysterectomy[6]. Intervention to limit tumor cell spillage and contamination of the peritoneal cavity during minimally invasive radical hysterectomy may therefore improve treatment outcomes. Recently, Kohler, et al[13] reported their experience in performing vaginally assisted laparoscopic radical hysterectomy with transvaginal closure of the vaginal cuff to avoid using a manipulator and potentially prevent tumor spillage. The 389 patients who underwent this operation were characterized using the same initial International Federation of Gynecology and Obstetrics stages as Ramirez, et al[6]. Kohler, et al[13] found that the 3-year OS and DFS of this cohort were equivalent to those of patients who underwent open radical hysterectomy in Ramirez, et al[6]. Vaginally assisted laparoscopic radical hysterectomy with transvaginal closure of the vaginal cuff seems to be oncologically safe in patients with early cervical cancer and its promising results should be validated in further randomized trials[13].

Unexpectedly, the rate parametrial involvement (13.4%) in this study was considerably high. Previous conducted in Thailand noted that parametrial involvement in women with early-stage cervical cancer was generally less than 5%[14]. This might raise the concern regarding the accuracy of clinical staging in our setting. Additionally, the rate of vaginal margin involvement in this study was 17.9% which was notably high. The high rate of vaginal margin involvement may indicate an inadequate radicality of vaginal excision during our LRH. The high rate of parametrial and vaginal margin involvement therefore may contribute to the high rate of adjuvant treatment given in our study population.

Our study has several drawbacks. First, it contained a relatively small sample size, which could be a factor precluding prognostic significance of the tumor size, as has been noted in previous reports[11, 12]. The relatively small sample size also precluded the ability of this study to determine the associations between the survival outcomes and various clinical factors i.e., patients' age, parity status, and minor pathological factors. The follow-up time in our series was also relatively short, which might influence the assessment of survival outcomes. Finally, the retrospective nature of this study impeded our ability to assess the homogeneous performance of the procedure conducted in our center.

Conclusion

In conclusion, the 5-year DFS and OS of patients undergoing LRH in this study were 75.4% and 76.8%, respectively, which were considerably lower than those previously reported for open radical hysterectomy. Patients with squamous cell carcinoma had longer survival than those with other histological types.

Potential conflicts of interest

The authors declare no conflicts of interest.

References

1. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. Cancer J Clin 2018;68:394-424.
2. Cibula D, Pötter R, Planchamp F, Avall-Lundqvist E, Fischerova D, Haie-Meder C, et al. The European Society of Gynaecological Oncology/European Society for Radiotherapy and Oncology/European Society of Pathology guidelines for the management of patients with cervical cancer. Virchows Archiv 2018;472:919-36.
3. Kietpeerakool C, Aue-aungkul A, Galaal K, Ngamjarus C, Lumbiganon P. Nerve-sparing radical hysterectomy compared to standard radical hysterectomy for women with early stage cervical cancer (stage Ia2 to IIa). Cochrane Database Syst Rev 2019;2:CD012828.
4. Verleye L, Vergote I, Reed N, Ottevanger PB. Quality assurance for radical hysterectomy for cervical cancer: the view of the European Organization for Research and Treatment of Cancer--Gynecological Cancer Group (EORTC-GCG). Ann Oncol 2009;20:1631-8.
5. Rydzewska L, Tierney J, Vale C, Symonds P. Chemoradiotherapy for Cervical Cancer Meta-analysis Collaboration (CCCMAC). Reducing uncertainties about the effects of chemoradiotherapy for cervical cancer: individual patient data meta-analysis. Cochrane Database Syst Rev 2010;1:CD008285.
6. Ramirez PT, Frumovitz M, Pareja R, Lopez A, Vieira M, Ribeiro R, et al. Minimally invasive versus abdominal radical hysterectomy for cervical cancer. N Engl J Med 2018;379:1895-904.
7. Melamed A, Margul DJ, Chen L, Keating NL, Del Carmen MG, Yang J, et al. Survival after minimally invasive radical hysterectomy for early-stage cervical cancer. N Engl J Med 2018;379:1905-14.
8. Cusimano MC, Baxter NN, Gien LT, Moineddin R, Liu N, Dossa F, et al. Impact of surgical approach on oncologic outcomes in women undergoing radical hysterectomy for cervical cancer. Am J Obstet Gynecol 2019;221:619.e1-e24.
9. Bhatla N, Berek JS, Fredes MC, Denny LA, Grenman S, Karunaratne K, et al. Revised FIGO staging for carcinoma of the cervix uteri. Int J Gynecol Obstet 2019;145:129-35.
10. Hongladaromp W, Tantipalakorn C, Charoenkwan K, Srisomboon J. Locoregional spread and survival of stage IIA1 versus stage IIA2 cervical cancer. Asian Pac J Cancer Prev 2014;15:887-90.
11. Mahawerawat S, Charoenkwan K, Srisomboon J, Khunamornpong S, Suprasert P, Sae-Teng CT. Surgical outcomes of patients with stage IA2 cervical cancer treated with radical hysterectomy. Asian Pac J Cancer Prev 2013;14:5375-8.
12. Srisomboon J, Kietpeerakool C, Suprasert P, Manopanya M, Siriaree S, Charoenkwan K, et al. Survival and prognostic factors comparing stage IB 1 versus stage IB 2 cervical cancer treated with primary radical hysterectomy. Asian Pac J Cancer Prev 2011;12:1753-6.
13. Kohler C, Hertel H, Herrmann J, Marnitz S, Mallmann P, Favero G, et al. Laparoscopic radical hysterectomy with transvaginal closure of vaginal cuff–a multicenter analysis. Int J Gynecol Cancer 2019;29:845-50.
14. Luengyosluechakul S, Temtanakitpaisan A, Kietpeerakool C, Chumworathayi B, Kleebkaow P, Aue-aungkul A, et al. Parametrial invasion in early-stage cervical cancer. Thai J Obstet Gynaecol 2020; 28:160-6.

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GYNAECOLOGY

Lidocaine Infiltration in Mesosalpinx for Reducing Operative Time in Postpartum Tubal Sterilization: A randomized, controlled trial

Vichunee Nithiwatthanasak, M.D.*,
Jesada Wutitammasuk, M.D.*

** Department of Obstetrics and Gynecology, Khon Kaen Hospital, Khon Kaen, Thailand*

ABSTRACT

Objectives: To evaluate the efficacy and dosage of lidocaine infiltration in mesosalpinx for reducing operative time in postpartum tubal sterilization.

Materials and Methods: A randomized, double-blinded, placebo-controlled trial was conducted in 105 women at Khon Kaen Hospital between April and July 2020. The participants were randomly assigned into three groups 4 ml of 2% lidocaine, 1% lidocaine, and normal saline solution (NSS) infiltrated in the mesosalpinx. Systemic sedative drugs were administered before the procedure in all groups. Operative time from skin incision to closure was recorded. Intra-operative, immediately and 1 hour post-operative pain score were evaluated.

Results: Age and body mass index were not statistically different between 2% lidocaine, 1% lidocaine, NSS groups (29.00 ± 4.54, 30.37 ± 5.92, 31.03 ± 5.08 yrs. and 25.08 ± 3.14, 25.88 ± 2.82, 26.08 ± 2.60 kg/m^2, respectively). Other baseline characteristics including postpartum duration before sterilization, parity, gestational age, and level of surgeon experience were similar across groups. Mean operative time for 2% lidocaine, 1% lidocaine, and NSS group was 17.9 ± 6.19, 21.6 ± 9.72, and 23.1 ± 12.04 min. The operative time of 2% lidocaine was significantly shorter than NSS ($p = 0.027$), and pain scores in 2% lidocaine were significantly lower than for NSS for all periods. The operative time of 1% lidocaine was not significantly different compared to NSS whereas 1% lidocaine had a significantly lower pain score only immediately and 1 hour post-operation. There were no serious adverse events found.

Conclusion: Two percent lidocaine infiltration in the mesosalpinx significantly shortened operative time and could reduce pain throughout postpartum tubal sterilization.

Keywords: lidocaine, mesosalpinx, postpartum, tubal sterilization, operative time, pain score.

Correspondence to: *Vichunee Nithiwatthanasak, M.D., Department of Obstetrics and Gynecology, Khon Kaen Hospital, Khon Kaen 40000, Thailand. E-mail: vichunee2527@gmail.com*

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การฉีดลิโดเคน (lidocaine) เข้าเนื้อเยื่อใต้ท่อนำไข่เพื่อลดระยะเวลาการผ่าตัดในการทำหมันหลังคลอด: การทดลองแบบสุ่ม

วิชชุณี นิธิวัฒนศักดิ์, เจษฎา วุฒิธรรมสุข

บทคัดย่อ

วัตถุประสงค์: *เพื่อศึกษาประสิทธิผลและขนาดของยาลิโดเคนในการฉีดเข้าเนื้อเยื่อใต้ท่อนำไข่เพื่อลดระยะเวลาการผ่าตัดในผู้ป่วยทำหมันหลังคลอด*

วัสดุและวิธีการ: *งานวิจัยนี้เป็นการศึกษาแบบสุ่ม ปกปิดทั้งสองฝ่าย ทำการศึกษาในหญิงหลังคลอด 105 คน ที่โรงพยาบาลขอนแก่น ระหว่างเดือนเมษายน ถึง กรกฎาคม พ.ศ.2563 โดยทำการสุ่มหญิงหลังคลอดแบ่งเป็น 3 กลุ่ม ได้แก่ กลุ่มที่ได้รับ 2% ลิโดเคน, กลุ่มที่ได้รับ 1% ลิโดเคน และกลุ่มที่ได้รับสารละลายน้ำเกลือ ปริมาณ 4 มิลลิลิตร โดยฉีดเข้าเนื้อเยื่อใต้ท่อนำไข่ โดยทุกกลุ่มได้รับยาระงับประสาททางหลอดเลือดดำก่อนทำหัตถการ บันทึกระยะเวลาการผ่าตัดตั้งแต่ลงแผลผ่าตัดจนเย็บปิดแผล บันทึกคะแนนความปวดในขณะผ่าตัด หลังเสร็จสิ้นการผ่าตัดทันที และหลังการผ่าตัด 1 ชั่วโมง*

ผลการศึกษา: *อายุและดัชนีมวลกายในกลุ่มที่ได้รับ 2% ลิโดเคน, กลุ่มที่ได้รับ 1% ลิโดเคน,กลุ่มที่ได้รับสารละลายน้ำเกลือไม่แตกต่างกันทางสถิติ (29.00 ± 4.54, 30.37 ± 5.92, 31.03 ± 5.08 ปี และ 25.08 ± 3.14, 25.88 ± 2.82, 26.08 ± 2.60 กก./ม^2 ตามลำดับ) ลักษณะพื้นฐานประชากรอื่นๆ ประกอบด้วย จำนวนการคลอด, อายุครรภ์, ระยะเวลาหลังคลอดก่อนการทำหมัน และระดับความชำนาญของแพทย์ผู้ผ่าตัด คล้ายคลึงกันในทุกกลุ่ม โดยระยะเวลาผ่าตัดเฉลี่ยของกลุ่ม 2% ลิโดเคน, 1% ลิโดเคน และ สารละลายน้ำเกลือ เท่ากับ 17.9 ± 6.19, 21.6 ± 9.72 และ 23.1 ± 12.04 นาที ตามลำดับ ซึ่งระยะเวลาในการผ่าตัดของกลุ่มที่ได้รับ 2% ลิโดเคน น้อยกว่ากลุ่มสารละลายน้ำเกลืออย่างมีนัยสำคัญทางสถิติ (p = 0.027) และคะแนนความเจ็บปวดในกลุ่มที่ได้รับ 2% ลิโดเคน น้อยกว่ากลุ่มที่ได้รับสารละลายน้ำเกลืออย่างมีนัยสำคัญทางสถิติในทุกช่วงเวลา ส่วนระยะเวลาการผ่าตัดเปรียบเทียบระหว่างกลุ่มที่ได้รับ 1% ลิโดเคน และกลุ่มที่ได้รับสารละลายน้ำเกลือไม่มีความแตกต่างกัน ในขณะที่กลุ่มที่ได้รับ 1% ลิโดเคน มีคะแนนความเจ็บปวดน้อยกว่ากลุ่มที่ได้รับสารละลายน้ำเกลืออย่างมีนัยสำคัญทางสถิติเฉพาะในช่วงหลังผ่าตัดทันทีและ 1 ชั่วโมงหลังการผ่าตัด ไม่พบเหตุการณ์ไม่พึงประสงค์ที่รุนแรง*

สรุป: *การฉีด 2% ลิโดเคน เข้าเนื้อเยื่อใต้ท่อนำไข่สามารถลดระยะเวลาการผ่าตัดได้อย่างมีนัยสำคัญทางสถิติและสามารถช่วยลดความเจ็บปวดตลอดการทำหมันหลังคลอด*

คำสำคัญ: *ลิโดเคน, เนื้อเยื่อใต้ท่อนำไข่, หลังคลอด, การทำหมันหญิง, ระยะเวลาการผ่าตัด, คะแนนความปวด์*

Introduction

Bilateral tubal sterilization is the most popular and effective permanent contraception method with a low rate of side effects[1]. Mini-laparotomy uses a small incision of about 2-3 cm placed either in relation to the uterine fundus or the infraumbilical site for postpartum sterilization[2], and requires only basic surgical instruments. This operation is appropriate for low-resource settings where specialized surgical equipment is not available[2]. Postoperative pain originates from three sources: the infraumbilical skin incision, the transection site, and the ligation site on the fallopian tubes[3]. This pain causes sensory and emotional discomfort and may also cause fear and anxiety perioperatively[4]. The inferior hypogastric nerves innervate the cervix, the body of the uterus, and the medial portion of each fallopian tube. The nerve plexus that runs along each ovarian artery innervates each ovary and the lateral portion of each fallopian tube. The suture ligation of a 2 cm segment of the fallopian tube may be transected or crush nerve endings from both medial and lateral nerve fibers. To reduce pain, the latter would require local anesthetic infiltration to both the medial and lateral transection sites on each fallopian tube to block afferent nociception[5].

Local anesthesia has proven to be the most appropriate anesthesia for mini-laparotomy. The aim of anesthesia is to reduce pain, anxiety, and to allow performance of a surgical procedure[6].

Lidocaine has fewer side effects, is inexpensive, potent, and readily available[1]. It blocks initiation and transmission of nerve impulses at the site of application by stabilizing the neuronal membrane[7]. Lidocaine is a moderately long-acting, local anesthetic, duration for 1-3 hours, onset within 1-5 min following mucosal application, infiltration, and spinal or dental nerve block[7]. The maximum dose of lidocaine for local infiltration is up to 400 mg[7].

In a previous study, lidocaine 40 mg was injected into the fallopian tubes compared with placebo to reduce pain. The result showed that the pain score was not significantly different between groups and might extend the operative time[8]. Long operative time may be due to patient intra-operative pain, so adequate pain control could reduce operative time. There is neither sufficient evidence nor any systematic reviews evaluating local anesthesia for operative time and pain reduction during tubal sterilization.

The current study was thus conducted to compare the efficacy of 80 mg vs. 40 mg of lidocaine, 80 mg lidocaine vs. normal saline (NSS), and 40 mg lidocaine vs. NSS infiltration in the mesosalpinx for reducing operative time during postpartum tubal sterilization. The secondary outcomes were pain score, adverse events, surgical complications, and patient satisfaction.

Materials and methods

This was a single center, double-blinded, randomized controlled trial. The subjects were postpartum women scheduled for tubal sterilization at Khon Kaen Hospital between April and July, 2020. Inclusion criteria were as follows: completed childbearing, no contraindication for surgery, had an American Society of Anesthesiologists (ASA) physical I and II[9], delivered within 72 hours before tubal sterilization, understood Thai language (speak, read, and write). Exclusion criteria were body mass index (BMI) ≥ 30 kg/m^2, lidocaine allergy, history of pelvic infection, and prior pelvic surgery. The study was reviewed and approved by the Khon Kaen Hospital Institute Review Board in Human Research (KEF62018). After obtaining written informed consent, all participants were randomized into three groups using a computer-generated program: the 2% lidocaine group, the 1% lidocaine group, and the normal saline group. The randomization lists were kept in sealed opaque envelopes.

All postpartum patients needed to fast for 6-8 hours prior to the tubal sterilization. Before the operation, numerical rating score (NRS) from

0-10[10] was used to evaluate the participant's understanding. The study was masked to the participants, surgeons, and nurses involved in the study. The sealed opaque envelopes were opened by a nurse who not involved in the study at the operative room and prepared the solutions for each group. The solutions were delivered with a 5 ml syringe containing 4 ml of 2% lidocaine, 4 ml of 1% lidocaine, and 4 ml of normal saline for each group, respectively. All solutions were transparent, and apparently identical without label.

The postpartum tubal sterilization was performed by all levels of residents or staff. Before the operation was started, all participants received a systemic sedative drug (morphine 0.1 mg/kg and diazepam 5 mg intravenously) and 20 ml of 1% lidocaine with adrenaline (1:100,000) infiltrated to the abdominal layer at the infra-umbilical site. A 2-cm transverse infra-umbilical incision was made. After approaching the intra-peritoneum, the fallopian tube was identified and held with Babcock forceps. As per the respective group assignment, 2 ml of solution was infiltrated into the avascular area of the mesosalpinx. After one minute of infiltration, tubal sterilization was performed using the Modified Pomeroy technique. The same procedure was performed on the other side so that a total of 4 ml of solution was given to each participant. The NRS was recorded thrice (a) immediately after resecting both sides of the fallopian tubes, (b) immediately after skin closure, and (c) 1 hour after surgery by a nurse not apprised of the study outcome measures.

Vital signs and pulse oximetry were monitored before, during, and after the operation to monitor for any local anesthetic, cardiovascular, respiratory emergencies. If any emergency events or intraoperative complications occurred, standard care and treatment were immediately administered.

We recorded operative time from skin incision to skin closure using standardized watch, which were recorded by a nurse not apprised of the study outcome measures. Adverse events, complications of surgery, and patient satisfaction (Likert scales) were recorded at 1 hour post-operation.

Statistical analyses were done using STATA version 13 software. The sample size calculation was based on the data of operative time from a pilot study of 10 participants in each group with an alpha of 0.05 and a beta of 0.2. Mean operative time for 2% lidocaine, 1% lidocaine, and NSS was 18.57 ± 7.25, 19.00 ± 3.82, and 24.57 ± 10.18 min. The total sample size was 35 participants per group. The operative time and pain score were presented as means ± standard deviation (SD) to compare between 2% lidocaine vs. 1% lidocaine, 2% lidocaine vs. NSS, and 1% lidocaine vs. NSS. Differences in continuous variables were analyzed using a one-way Analysis of Variance (ANOVA). Categorical variables were analyzed using chi-squared and Fisher's exact test as appropriate. Continuous variables were analyzed using the independent t-test presented as mean differences and 95% confidence intervals (CI). A p value < 0.05 was considered statistically significant.

Results

One hundred and nineteen postpartum women were assessed for eligibility. Fourteen women were excluded: 12 had a BMI ≥ 30 kg/m^2, and 2 declined to participate. One hundred and five women were randomized into 3 groups: the 2% lidocaine group, the 1% lidocaine group, and the normal saline group: 35 per group (Fig. 1). Data recorded included age, BMI, postpartum duration before sterilization, gestational age (GA), parity, levels of surgeon experience, operative time, pain score, side effects, patient satisfaction, and complications of surgery.

Baseline characteristics of the participants were presented in Table 1. There were no statistically significant differences between the three groups with respect to age, BMI, postpartum duration before sterilization, GA, parity, and levels of surgeon experience ($p > 0.05$).

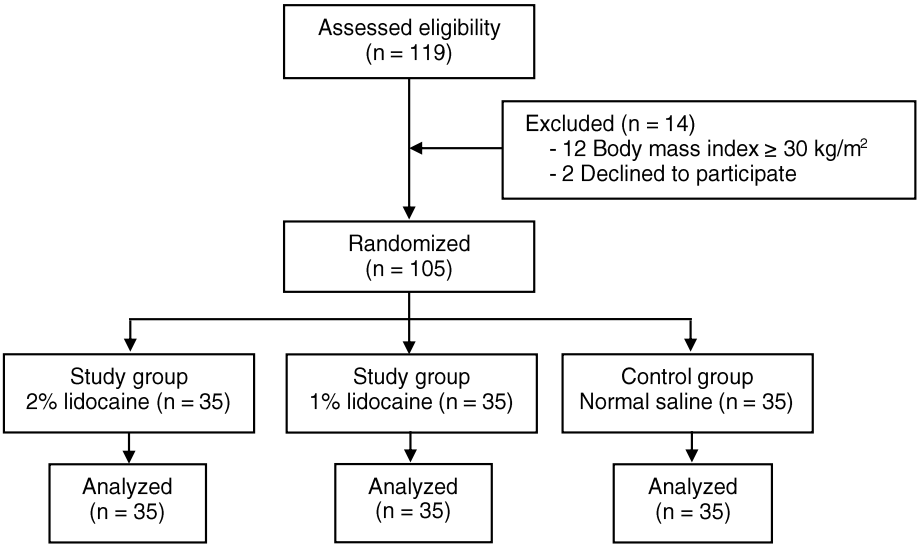

Fig. 1. Study flow diagram.

Table 1. Baseline characteristics.

	1% Lidocaine (n = 35)	2% Lidocaine (n = 35)	Normal saline (n = 35)	p value
Age (years), mean ± SD	29.00 ± 4.54	30.37 ± 5.92	31.03 ± 5.08	0.26[a]
BMI (kg/m^2), mean ± SD	25.08 ± 3.14	25.88 ± 2.82	26.08 ± 2.60	0.31[a]
Postpartum (hours), mean ± SD	42.11 ± 19.22	36.57 ± 18.46	34.86 ± 16.24	0.22[a]
GA (days), mean ± SD	268.89 ± 12.02	271.37 ± 8.50	267.89 ± 7.60	0.30[a]
No. of gravida				
Parity, n (%)				0.93[b]
2	23 (65.7)	22 (62.9)	26 (74.2)	
3	10 (28.5)	10 (28.5)	8 (22.9)	
4	1 (2.9)	2 (5.7)	1 (2.9)	
5	1 (2.9)	1 (2.9)	0 (0.0)	
Surgeon, n (%)				0.72[b]
Resident 1	15 (42.9)	16 (45.7)	6 (45.7)	
Resident 2	11 (31.4)	12 (34.3)	8 (22.9)	
Resident 3	0 (0.0)	0 (0.0)	2 (5.7)	
Staff	9 (25.7)	7 (20.0)	9 (25.7)	

[a] One way ANOVA, [b] Fisher's exact test

SD: standard deviation, BMI: body mass index, GA: gestational age

The respective mean operative time for the 2% lidocaine, 1% lidocaine, and NSS group was 17.9 ± 6.19, 21.6 ± 9.72, and 23.1 ± 12.04 min (Fig. 2). Operative time for the 2% lidocaine group was significantly less than that for the NSS group (mean difference = -5.17 min, 95%CI -9.74 to -0.61, p =

0.027). There were no significant differences between the 1% lidocaine group and the NSS group (mean difference = -1.43 min, 95%CI -6.65 to 3.79, p = 0.587) and the 2% lidocaine and the 1% lidocaine group (mean difference = -3.74 min, 95%CI -7.63 to 0.14, p = 0.059) (Fig. 2).

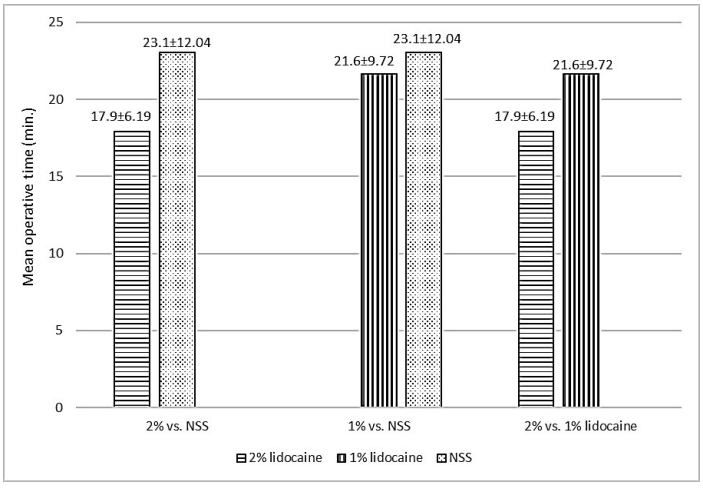

Fig. 2. Mean operative time.

Pain scores in the 2% lidocaine group were significantly lower than those of the NSS group for all periods (i.e., the respective intra-operative; immediate post-operative; and, 1 hour post-operative mean difference was -2.29, 95%CI -3.45 to -1.12, p < 0.001; -2.94, 95%CI -4.12 to -1.77, p < 0.001; and -2.74, 95%CI -3.87 to -1.62, p < 0.001) (Fig. 3). By comparison, the 1% lidocaine group had a significantly lower pain score than that of the NSS group (i.e., the respective immediate post-operative and 1 hour post-operative mean difference was -1.43 (95%CI -2.54 to -0.32, p = 0.012) and -1.94 (95%CI -3.09 to -0.79, p = 0.001) (Fig. 3). The 2% lidocaine group had a lower pain score than that of the 1% lidocaine group (i.e., the respective intra-operative and the immediate post-operative mean difference was -1.34 (95%CI -2.50 to -0.18, p = 0.024) and -1.52 (95%CI -2.75 to -0.28, p = 0.017) (Fig. 3). The mean pain score showed that increasing the concentration of lidocaine could reduce the pain score (Fig. 3).

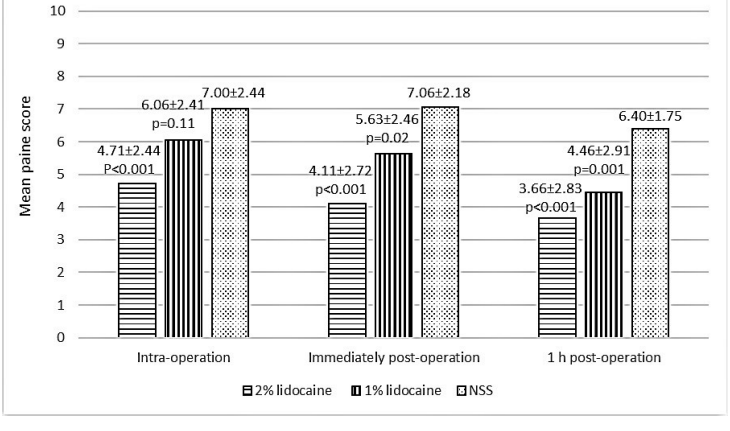

Fig. 3. Mean pain score.

There were no statistically significant differences between the three groups with respect to side effects, patient satisfaction without complications of surgery ($p > 0.05$) (e.g., bleeding, hematoma, and tear mesosalpinx) (Table 2).

Table 2. Side effects and patient satisfaction.

	1% Lidocaine (n = 35)	2% Lidocaine (n = 35)	Normal saline (n = 35)	p value
Side effects, n (%)				
Nausea and vomiting	0 (0.0)	1 (2.9)	1 (2.9)	0.61[b]
Headache	2 (5.7)	2 (5.7)	0 (0.0)	0.55[b]
Tremor	1 (2.9)	0 (0.0)	0 (0.0)	0.37[b]
Dizziness	2 (5.7)	0 (0.0)	1 (2.9)	0.78[b]
Numbness and tingling	0 (0.0)	0 (0.0)	0 (0.0)	N/A
Patient satisfaction, n (%)				0.07[b]
Poor	0 (0.0)	0 (0.0)	0 (0.0)	
Fair	0 (0.0)	0 (0.0)	0 (0.0)	
Good	1 (2.9)	2 (5.7)	1 (2.9)	
Very good	13 (37.1)	10 (28.6)	21 (60.0)	
Excellent	21 (60.0)	23 (65.7)	13 (37.1)	

[b] Fisher's exact test
N/A: non applicable

Discussion

The current randomized, double-blinded, placebo-controlled trial evaluated the effectiveness of lidocaine infiltration in the mesosalpinx for reducing operative time in postpartum tubal sterilization. We found that 2% lidocaine reduced operative time in postpartum sterilization, but 1% lidocaine yielded no greater effectiveness compared to placebo. The operative time may reflect the surrogate outcome of pain control during operation proxied by more patient cooperation and resulting in a shorter operative time. Generally, during the search for each fallopian tube, the patient is asked to pull in the stomach so as (a) to pull down the abdominal wall close to the uterus and (b) the bowels not obscure the view. In cases where the patient suffers from pain during tubal ligation and transection of the first side, the patient may push out the abdomen causing the bowels to come down which can interfere with the operative field. In such cases, there is a need for deep force (i.e., abdominal traction or bowel packing) to expose the surgical field which can increase the operative time. There are other factors that can affect operative time such as intra-abdominal tissue traction due to thickness of the abdominal wall, fundal height, parity, and surgeon experience. Participant BMI, postpartum duration before sterilization, parity, and level of surgeon skill were not statistically significant differences in the current study.

The current study showed that 2% lidocaine was able to significantly reduce pain to a mild to moderate pain score throughout postpartum tubal sterilization until 1 hour post-operation whereas 1% lidocaine only reduced pain to a moderate pain score immediately and 1 hour post-operation compared to NSS. The result confirmed that intravenous sedative drug and local abdominal infiltration with lidocaine during tubal

sterilization did not adequately control pain. Our findings were comparable to those of Songserm et al[8], who reported that 1% infiltrated lidocaine provided no better intra-operative pain relief than normal saline infiltrated into mesosalpinx of the fallopian tubes. In the current study, participants received low doses of systemic sedative drug during tubal sterilization so that all participants remained consciousness and able to assess their pain score.

To our knowledge, there has been no previous study comparing operative time as a primary outcome. Several studies have evaluated the effectiveness of lidocaine for reducing intra-operative pain as a primary outcome; however, pain measurement is subjective and there are many idiosyncratic factors that can affect the level of pain (e.g., individual pain threshold and experience of pain).

The strength of our study was that it was a double-blinded, randomized, controlled trial. The limitation of the study was that the duration of operative time might be affected by abdominal wall thickness, fundal height, and the level of surgeon experience.

Conclusion

Two percent lidocaine infiltration in the mesosalpinx significantly shortened operative time and reduced operative pain in postpartum tubal sterilization without any serious adverse events.

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Potential conflicts of interest

The authors declare no conflict of interest.

References

1. Arab M, Manochehrian N, Mehrangiz Z. The effect of bupivacaine infiltration on postoperative tubal-ligation pain. Internet J Pain Symptom Control Palliative Care 2003;3:31-6.
2. American College of Obstetricians and Gynecologists. ACOG Practice bulletin no. 133: Benefits and risks of sterilization. Obstet Gynecol 2013;121:392-404.
3. Wittels B, Faure EAM, Chavez R, Moawad A, Ismail M, Hibbard J, et al. Effective analgesia after bilateral tubal ligation. Anesth Analg 1998;87:619-23.
4. Shivanna P, Raghuram S. Effect of pre-incisional and mesosalpinx infiltration of local anaesthesia for post-operative analgesia in bilateral abdominal tubectomies-a randomized placebo-controlled study. J Evid Based Med Healthc 2017;4:2437-42.
5. Sokol E. Clinical anatomy of the uterus, fallopian tubes, & ovaries. The Global Library of Women's Medicine [internet]. 2009 [cited 2019 Jun 26]. Available from: https://www.glowm.com/section_view/item/1
6. Jacobstein R, ed. Minilaparotomy for female sterilization. 1st ed. New York: Automated graphic systems 2003: 25-37.
7. World Health Organization. WHO model prescribing information: drugs used in anaesthesia: local anaesthetics. Geneva: World Health Organization 1989.
8. Songserm V, Werawatakul Y, Sothornwit J, Prasit M, Thongpha S. Lidocaine injection in mesosalpinx for pain relief during post-partum tubal sterilization in Srinagarind Hospital: A randomized controlled trial. Thai J Obstet Gynaecol 2017;25:11-7.
9. American Society of Anesthesiologists. ASA Physical Status Classification System 1995 [cited 2019 Jun 26].
10. Wysham NG, Miriovsky BJ, Currow DC, Herndon JE, Samsa GP, Wilcock A, et al. Practical dyspnea assessment: relationship between the 0-10 numerical rating scale and the four-level categorical verbal descriptor scale of dyspnea intensity. J Pain Symptom Manage 2015;50:480-7.

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OBSTETRICS

Prediction of the Mode of Delivery using Intrapartum Translabial Ultrasound in a Teaching Hospital in South India – A prospective observational study

Vinutha MB, MBBS, DGO, Secondary DNB.*,
Vinutha Vinod, MBBS, DGO, DNB.*
Chitra Kotian, BDS, MPH.*,
Krupa Shah, MBBS, M.D.*,
Shashikala K Bhat, MBBS, M.D.*

** Department of Obstetrics and Gynecology, DR. TMA Pai Hospital, Udupi, Melaka Manipal Medical College, Manipal Academy of Higher Education, Karnataka, India*

ABSTRACT

Objectives: Cervical effacement and dilatation, station of the presenting part, and fetal head position are the key determinants of progress of labor. There is growing evidence about the usefulness of intrapartum ultrasound in evaluating the labor parameters objectively to decide about the labor management. Hence, intrapartum translabial ultrasound was studied to predict the mode of delivery.

Materials and Methods: 185 laboring women with singleton pregnancy, term gestation, and cephalic presentation with 4 cm. cervical dilatation were included. Intrapartum translabial ultrasound was done to note angle of progression (AoP), cervical length, and position of the fetal head.

Results: Among 185 women, 121 (65.4%) had vaginal (112 normal and 9 assisted vaginal) and 64 cesarean (34.6%) delivery. An angle of progression of 89° with area under the curve (AUC) 0.789 ($p \leq 0.0001$) measured in the early active phase of labor had a sensitivity, specificity, positive predictive value and negative predictive value of 79.3% and 65.6%, 81.3% and 62.7% respectively. The positive likelihood ratio and the negative likelihood ratio were 2.3 and 0.315, respectively. The clinical utility index for AoP was 0.644 in predicting the mode of delivery. AUC for cervical length was 0.534 ($p = 0.452$), which was not significant. The odds ratio for occipitoanterior position in predicting vaginal delivery was 3.9.

Conclusion: Intrapartum translabial ultrasound is a reproducible and feasible method to evaluate labor parameters. Assessing multiple components like the angle of progression, cervical length, and position of the fetal head in early labor could help to predict the mode of delivery.

Keywords: angle of progression, cervical length, mode of delivery, position of fetal head, intrapartum translabial ultrasound.

Correspondence to: *Shashikala K Bhat, M.D., Department of Obstetrics and Gynecology, DR. TMA Pai Hospital, Udupi, Melaka Manipal Medical College, Manipal Academy of Higher Education, Karnataka, India Email: shashikala.bhat@manipal.edu*

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Introduction

Cervical effacement and dilatation, station of the presenting part, and fetal head position are the key determinants of labor progress. Progress of labor has been evaluated clinically by transvaginal digital examination traditionally. Ultrasound has become an useful investigation in the labor rooms in the current day practice[1,2]. Novel intrapartum ultrasound techniques[3,4] were introduced for to determine position[5] and station, especially before an instrumental delivery when the presence of caput succedanum jeopardizes the clinical judgment[6]. Angle of progression (AoP) is one of the most reliable parameters to predict the mode of delivery[7-9]. Intrapartum ultrasound shows high diagnostic accuracy in determining engaged fetal head at angle of progression of ≥ 101° [10] and also indicates the trends in the duration of labor[11]. Intrapartum abdominal and transperineal ultrasound parameters using head station, cervical dilatation, and AoP have found clinical applicability to predict labor[12]. Transperineal ultrasound has been found useful even after full cervical dilatation to predict vaginal delivery and is a useful reproducible adjunct to determine position and station, especially before an instrumental delivery[13]. The images obtained by ultrasound can be stored in medical records. Identifying women are at risk for cesarean delivery helps in improving pregnancy outcomes by avoiding unplanned emergency cesarean section and improves childbirth experience. Hence, we set out to study the role of intrapartum translabial ultrasound (ITU) with the mode of delivery. The primary objective was to study the role of AoP, cervical length, and position of the fetal head in predicting the mode of delivery in early labor. The secondary objective was to establish a cut-off value for AoP to predict the mode of delivery.

Materials and Methods

This was a prospective observational study conducted from April 2019 to November 2019 in the Department of Obstetrics and Gynaecology, Dr. TMA Pai Hospital, Udupi. The study population consisted of women in labor admitted in Dr TMA Pai Hospital, Udupi, and fulfilling the inclusion criteria. Women in established labor (cervical dilatation of 4cm) with live, singleton pregnancy at term in cephalic presentation were included. Those with multiple gestation, malpresentation, previous cesarean delivery, uterine surgeries and anomalous uterus were excluded. Anticipating 95% confidence interval, 5% error margin, a sample size of 185 was calculated based on a study by Perez, et al[8], wherein area under the curve for AoP was 0.85 (95% confidence interval 0.77-0.92). Institutional Ethical Committee clearance was obtained (KH IEC number: 105/2019) and CTRI (Clinical Trial Registry India) registration (CTRI/2019/04/018508) was done. Informed consent was obtained from the subject after explaining the study and F form was documented as per regulatory requirements by the government of India.

Ultrasonography was performed when cervical dilatation was 4 cm. Translabial ultrasound was carried out using either PHILIPS CLEARVUE 350 or SONOSITE M-TURBO ultrasound machine with 5MHz curvilinear transducer c5-2. Subjects were put in dorsal position with an empty urinary bladder. The ultrasound probe was enclosed in a latex disposable glove covered with ultrasound gel.

For the AoP, the probe was placed vertically between labia below the pubic symphysis in the midsagittal plane. An image where the long axis of the pubic symphysis and the leading portion of the fetal head could be made out was obtained. A line was drawn between callipers placed at two ends of the long axis of pubic symphysis (a). The second line was drawn from distal point of the pubic symphysis tangentially to the fetal skull contour (b). AoP was measured manually[2,14] (Fig. 1).

Measurement of cervical length was done in sagittal plane. It was measured from internal os to the external os[15] (Fig. 2). Three measurements were taken, and the average of the 3 measurements was noted.

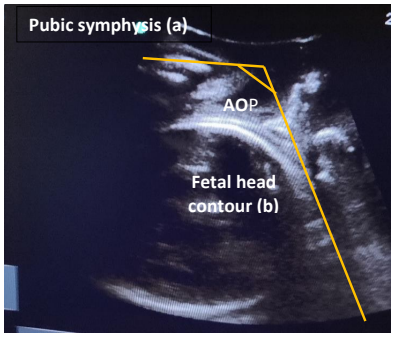

Fig. 1. Sagittal view for measuring angle of progression.

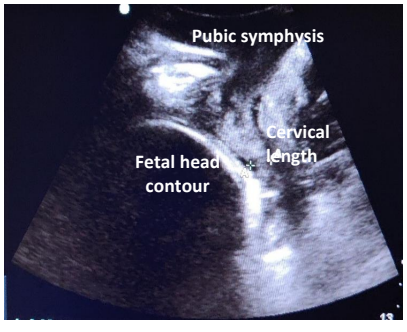

Fig. 2. Sagittal view showing cervical length.

Ultrasound assessment of the fetal head position was done by swinging the transducer across the axial and sagittal planes. The position was assessed utilizing the midline intracranial structures (cavum septum pellucidum, falx cerebri, thalamus, and cerebellar hemispheres) and anterior or posterior cranial structures (orbits, nasal bridge and cervical spine). Position was described by depicting a circle, like a clock. Depiction of fetal occiput based on hour hand on a clock: positions 2:00 and 4:00 hours were recorded as left occiput transverse (LOT); positions 8:00 and 10:00 hours as right occiput transverse (ROT); positions from 4:00 and 8:00 hours as occiput posterior; and positions 10:00 and 2:00 hours as occiput anterior (Fig. 3).

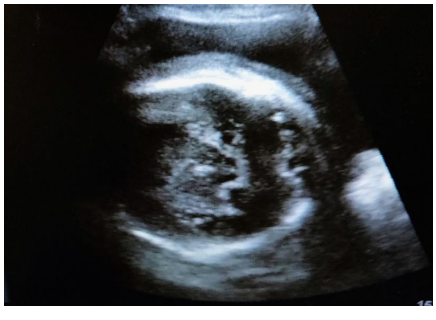

Fig. 3. Ultrasound image of left occipito-transverse position.

The primary outcome measure was to predict the mode of delivery using AoP, cervical length, and position of the fetal head by translabial ultrasound. The secondary outcome was to determine the cut off value of the AoP to predicting vaginal delivery.

Data were entered in Microsoft Excel datasheet and analyzed using Scientific Package for Social Sciences (SPSS) 20 software. Analysis of demographic data was done using percentages for categorical data, mean and standard deviation for continuous data. Analysis of the AoP was done by receiver operating characteristics (ROC) curve. Sensitivity, specificity, positive predictive value and negative predictive value were measured. Cut-off value of AoP, likelihood ratios and clinical utility index were calculated. The area under the curve (AUC) for cervical length was measured. Odds ratio for position of fetal head was calculated. Logistic regression analysis for all the variables was calculated. P value < 0.05 was considered to be statistically significant.

Results

185 laboring women were enrolled in the study. There were 121 vaginal (65.4%) and 64 cesarean (34.6%) deliveries. Among 121 vaginal deliveries, 112 were normal, and nine were assisted vaginal deliveries. Table 1 presents the demographic and clinical characteristics of the study population. Nulliparous women constituted almost three fourth (74.1%) of the study population.

Table 1. Demographic profile of the study population.

Characteristics	n = 185
Maternal age* (years)	27 ± 3
Parity	
Nulliparous** (%)	74.1
Multiparous** (%)	25.9
Gestational age* (weeks)	38 ± 0.9
Body mass index (kg/m^2)***	22 (20-26)
Birth weight* (kg)	2.9 ± 0.3

Data are presented as mean ± standard deviation* or n (%)** or median (interquartile range)***

Angle of progression (AoP)

Table 2 depicts the mean AoP, cervical length and position of fetal head in early labor (4cm of cervical dilatation) and mode of delivery. It was observed that as the AoP increased, the chance of vaginal delivery increased. More women with higher AoP delivered vaginally (Fig. 4), whereas only one-fourth women delivered vaginally when AoP < 80^o.

Table 2. Angle of progression, cervical length and position of fetal head in early labour (4cm. of cervical dilatation) and mode of delivery.

Predictors	Vaginal delivery n = 121	Caesarean n = 64
Angle of progression* (^{o})	106 ± 21.9	85.2 ± 14.9
Cervical length* (millimetre)	13.6 ± 5.5	14.7 ± 6.1
Occipito-anterior position** (%)	83.6	16.4
Other positions** (%)	56.5	43.5

* Angle of progression and cervical length are mentioned as mean ± standard deviation.
**Position of the fetal head is mentioned as n (%)

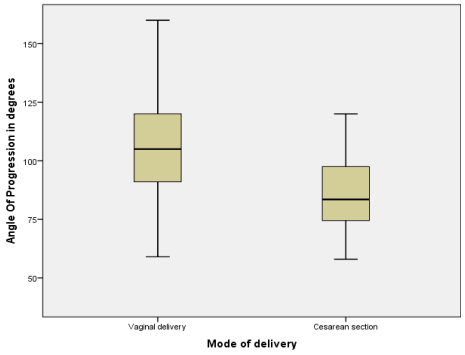

Fig. 4. Angle of progression measured by intrapartum translabial ultrasound. Median angle of progression was 83.5° (IQR 74.5-97.5) in women who had cesarean delivery which was narrower compared to angle of progression in women who had vaginal delivery (105° (IQR 91-120)).

Fig. 5 represents the ROC curve with an AUC of 0.789 (95% CI 0.723-0.855) for AoP in vaginal delivery (both spontaneous vaginal and assisted vaginal delivery). An AoP ≥ 89° was associated with vaginal delivery in 81.4% (96 out of 118), and an AoP < 89° was associated with 62.9% (42 out of 67) risk for caesarean delivery. The value of AoP that optimized the curve was 89° (p ≤ 0.0001). An AOP of 89° measured in the early active phase of labor had a sensitivity, specificity, positive predictive value, and negative predictive value of 79.3%, 65.6%, 81.3% and 62.7%, respectively. The positive likelihood ratio and the negative likelihood ratio were 2.3 and 0.315, respectively. In primigravid women, with a cut-off value of 89°, the AUC was 0.794. The sensitivity was 80.8%, specificity was 63% (p < 0.0001). In multigravida women, AUC was 0.816 for 94.5° cut-off AoP, with sensitivity 72%, specificity 80% (p = 0.022). The Clinical Utility Index was 0.644, indicating that AoP has good utility (CUI ≥ 0.64) in predicting the mode of delivery.

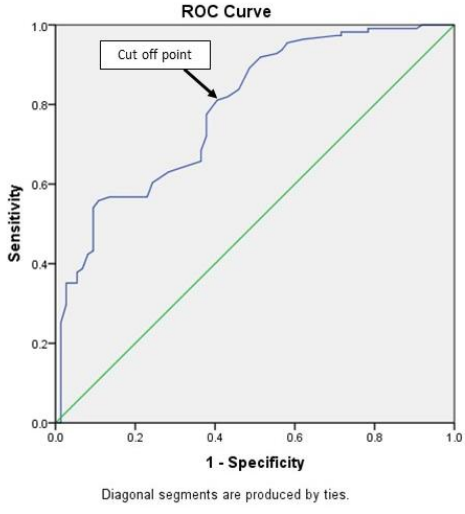

Fig. 5. Receiver operating characteristics curve for angle of progression measured in early active phase of labour in predicting vaginal delivery (AUC=0.789, p ≤ 0.0001) at cut off of 89°.

Cervical length

Though the chance of vaginal delivery increased as cervical length decreased, cervical length measured by ITU was not a good predictor of the mode of delivery, as shown in Fig. 6.

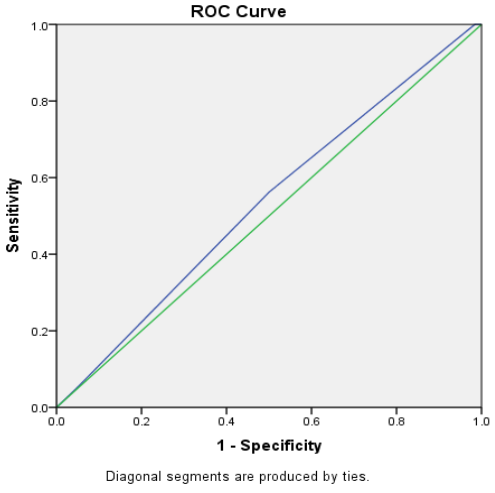

Fig. 6. Receiver operating characteristics curve for cervical length measured in early labour in predicting vaginal delivery (AUC = 0.534, p = 0.452).

Position of fetal head

Odds ratio for occipito-anterior position in predicting vaginal delivery was 3.9. Sensitivity for occipito-anterior position in predicting vaginal delivery was 42.42% and specificity was 84.3%. But the diagnostic accuracy of fetal head position in early labor in predicting the mode of delivery was only 0.56.

Table 3 represents the results of binomial logistic regression analysis. After taking all variables into account in the analysis, AoP, occipito-anterior position of fetal head, and parity were the significant predictors of mode of delivery.

Table 3. Summary of binominal logistic regression analysis of all the variables in predicting the mode of delivery.

Variable	Adjusted odds ratio (95%CI)	p value
Angle of progression (°)	0.938 (0.915 -0.962)	< 0.0001
Cervical length (millimetre)	2.702 (0.481-15.166)	0.259
Occipito-anterior position	2.696 (1.034-7.035)	0.043
Age (years)	0.937 (0.845-1.039)	0.218
Parity	7.244 (2.230-23.528)	0.001
Period of gestation (weeks)	0.770 (0.501-1.183)	0.233
Body Mass Index (kg/m^2)	1.056 (0.959-1.163)	0.269
Birth weight (kg)	1.000 (0.999-1.001)	0.708

CI: confidence interval

Discussion

Intrapartum ultrasound allows objective and reproducible measurement of labor parameters and is comparable to digital vaginal examination, is non-invasive and does not cause discomfort[16,17]. With increasing resolution and easier accessibility, ultrasound is used for fetal head status (engagement, station, and position), cervical status (shortening and dilatation) and placental separation to make more reliable clinical decisions[18]. Fetal head position can be identified by transabdominal, transperineal, and translabial ultrasound to diagnose malposition in labor dystocia, especially in the second stage of labour before instrumental delivery. In recent times, intrapartum ultrasound has been used to predict the mode of delivery using one or more parameters involving cervix, station, and position of the fetal head. In this study, we showed that ITU in early labor could provide reliable measurements for predicting labor outcome.

Ultrasound determined AoP in predicting the mode of delivery

185 laboring women were included in the study population. We observed that as the AoP increased, the number of vaginal deliveries increased. With AoP ≤ 80°, 75% had cesarean delivery, and when AoP >120°, all deliveries were vaginal. Results of our study were comparable with studies by Kalache, et al[19] and Barbera, et al[4] in 2009 which concluded that when AoP was >120°, there was higher probability of vaginal delivery[19]. An angle of 99°-120° correlated with zero station[20,21]. By using transperineal ultrasound, the AoP of 95° corresponded to -2 station and 116° to 0 station[22].

A prospective observational study was done by Levy et al in 2012 on 100 primiparous women who were not in labor, where AoP was measured by transperineal ultrasound. The AUC for the AoP was 0.878 ($p < 0.001$) with the cut-off angle of 95°. This cut-off angle had a sensitivity of 85%, a specificity of 89%, a positive predictive value of 98.7% and a negative predictive value of 86.3%. The positive likelihood ratio was 7.7 in predicting vaginal delivery[23]. AoP > 92° in non-laboring nulliparous women at term was associated with 94.8% vaginal delivery[24]. In a study by Minajagi et al in 120 nulliparous women, the AoP > 96° was associated with vaginal delivery in 95% (76/80) of women[25]. In a study by Kohl's et al, the mean AoP was 100.9° at cervical dilation < 5 cm and 125.3° at cervical dilatation > 5 cm in spontaneous vaginal deliveries. In assisted vaginal deliveries, it was 93° at < 5cm cervical dilatation and 113.9° when > 5 cm[11].

Study by Perez et al established an AUC of 0.85 with a cut-off angle of 125° with a sensitivity of 67.1% and maximum (100%) specificity. The cut-off angle established by this study was much higher than the current study[8].

Studies by Eggebo, et al[26] and Torkildsen, et al[27] were comparable to the current study with respect to the AUC of 0.75 and 0.76, respectively. The cut-off angle was 110° in both the studies. Unlike the current study, both these studies showed low sensitivity and specificity. Positive predictive value and likelihood ratios of both the studies were comparable to the present study. The odds ratio of the current study was 7.7, and it was comparable to studies by Eggebo et al (OR = 5.5) and Torkildsen et al (OR = 1.09).

Ultrasound determined cervical length in predicting the mode of delivery

In our study, translabial ultrasound was performed in all 185 study population in early labor and the cervical length was measured. Majority of the study population had a cervical length between 11 to 20 mm (55.13%) irrespective of parity. As the cervical length decreased, the chance of vaginal delivery increased with 77.8% vaginal delivery when the cervical length was < 11 mm. Tan et al compared cervical length measured by transvaginal ultrasound with Bishop score in predicting cesarean delivery. They showed that cervical length > 20 mm prior to induction was an independent predictor of cesarean delivery[28].

ROC curve for cervical length in labor showed an AUC of 0.534 ($p = 0.452$). Thus, it cannot be used as a predictor for the mode of delivery. Results of our study were comparable to study by Hamide et al in

2018, where cervical length measured by transvaginal ultrasound failed to predict the mode of delivery (p = 0.79)[29]. In a study by Alanwar et al, the cervical length measurement by transvaginal ultrasonogram had poor predictive value for cesarean delivery (AUC = 0.694)[30].

In a systematic review and meta-analysis by Verhoeven et al, summary estimates of sensitivity/ specificity for 20, 30 and 40 mm cervical length by ultrasound were 0.82/0.34, 0.64/0.74 and 0.13/0.95 prior to induction of labor suggesting ROC with poor predictive value for caesarean delivery[31]. Study by Khazardoost et al in 2016 showed an AUC of 0.628 (p = 0.034)[32].

In contrast to the results of the present study, Aggarwal et al (2019) measured cervical length by transvaginal ultrasound in 300 women, which showed a significant (p < 0.001) AUC of 0.72. They established a cut-off value of ≤ 3.4 cm for predicting successful induction of labor with sensitivity and specificity of 82% and 87%, respectively[33]. The difference is likely because our study was done in early labor and this study was done prior to induction of labour.

Ultrasound determined position of fetal head in predicting the mode of delivery

The odds ratio for the occipito-anterior position in early labor was 3.9. The diagnostic accuracy of fetal head position in early labor in predicting the mode of delivery was 0.56. Determining the position of the fetal head is of utmost importance in labor dystocia. Occipito-posterior position was associated with the prolonged first and second stage of labor, higher risk of assisted vaginal delivery and increased maternal and perinatal morbidity. Determining fetal head position is a prerequisite for instrumental delivery. An error in the evaluation may result in the inappropriate placement of vacuum or forceps, increasing the risk of injury to fetus and its failure. Wiafe et al concluded that ultrasound was better than digital vaginal examination to identify malposition in first stage of labor[34].

In all 185 subjects, fetal head position was assessed by translabial ultrasound in early labor. Fetal head position was anterior in 61 cases (32.97%) and among them, vaginal delivery was in 83.6% (51 out of 61), compared to vaginal delivery of 53.2% (66 out of 124) with other fetal head positions. When the position of the fetal head in early labor was occipito-anterior, the odds ratio of having vaginal delivery was 3.9 times more than that of cesarean delivery (p = 0.042).

The results of our study were comparable to the study conducted by Eggebo et al in 2015 on 150 women in the first stage of labor. They showed a significant odds ratio of 2.9 for predicting cesarean delivery with occipito-posterior position (p = 0.02)[35]. Choi et al (2013) conducted a study on 101 primiparous women using ultrasound in both first and second stage of labor. They concluded that the rate of cesarean delivery in the occipito-posterior position was significantly higher than those in occipito-anterior (p = 0.0024) and transverse position (p = 0.0374). In another study, Choi in 2016 showed that occipito-posterior position was associated with a longer duration of labor than non- occipito-posterior group (77.9 ± 33.4 min versus 52.2 ± 26.6 min, p = 0.0104)[36]. A study by Akmal et al in 2004 on 601 patients by transabdominal ultrasound in active labor showed that fetal head position can predict mode of delivery (odds ratio 2.2, p ≤ 0.001)[37]. However, a meta-analysis of 11 studies between 1999 and 2012 by Verhoeven et al concluded that position determined by ultrasound could not be used as a predictor of the mode of delivery as summary point estimates of sensitivity and specificity were 0.39 and 0.71[38].

The current study showed a significant correlation between the AoP and position of the fetal head and poor correlation between cervical length and mode of delivery. A risk score based on maternal age, body mass index, and gestational age with intrapartum ultrasound parameters can better predict vaginal delivery (AUC 0.853) in nulliparous women in the first stage of labor[39]. ITU can also be used for teaching students about the dynamic assessment of these key components in labor.

This is the first study in this region using composite ultrasound parameters (AoP, cervical length and position of fetal head) in labor to predict the mode of delivery. However, the small sample size of the study, manual measurement of AoP were the limitations. Serial measurements of AoP and position of the fetal

head would aid in easy decision making in cases of non-progress of labour.

Conclusion

Intrapartum translabial ultrasound can be used as a suitable alternative method to the traditional digital vaginal examination in assessing cervical length, descent of head and position of the presenting part in labor. AoP, the most reproducible ultrasound parameter, which quantifies descent of fetal head, and position of the fetal head assessed by translabial ultrasound in early labor can be used to predict the mode of delivery. The probability of vaginal delivery increases as the AoP increases, with most women delivering vaginally if the AoP is > 120°. Cervical length by ITU is not a good predictor of the mode of delivery. ITU can be used as a primary modality in initial labor assessment or as an additive tool to digital vaginal examination. Large, prospective, multicentric, observational studies are required to justify the routine use of intrapartum ultrasound in the Indian context.

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Potential conflicts of interest

The authors declare no conflict of interest.

References

1. Siergiej M, Sudoł-Szopińska I, Zwoliński J, Śladowska-Zwolińska AM. Role of intrapartum ultrasound in modern obstetrics – current perspectives and literature review. J Ultrason 2019;19:295-301.
2. Ghi T, Eggebø T, Lees C, Kalache K, Rozenberg P, Youssef A, et al. ISUOG Practice Guidelines: intrapartum ultrasound. Ultrasound Obstet Gynecol 2018;52:128-39.
3. Dietz HP, Lanzarone V. Measuring engagement of the fetal head: validity and reproducibility of a new ultrasound technique. Ultrasound Obstet Gynecol 2005;25:165-8.
4. Barbera AF, Pombar X, Perugino G, Lezotte DC, Hobbins JC. A new method to assess fetal head descent in labor with transperineal ultrasound. Ultrasound Obstet Gynecol 2009;33:313-9.
5. Adam G, Sirbu O, Voicu C, Dominic D, Tudorache S, Cernea N. Intrapartum ultrasound assessment of fetal head position, tip the scale: natural or instrumental delivery? Curr Health Sci J 2014;40:18-22.
6. Malvasi A, Tinelli A, Barbera A, Eggebø TM, Mynbaev OA, Bochicchio M, et al. Occiput posterior position diagnosis: vaginal examination or intrapartum sonography? A clinical review. J Matern Neonatal Med 2014;27:520-6.
7. Dückelmann AM, Bamberg C, Michaelis SAM, Lange J, Nonnenmacher A, Dudenhausen JW, et al. Measurement of fetal head descent using the 'angle of progression' on transperineal ultrasound imaging is reliable regardless of fetal head station or ultrasound expertise. Ultrasound Obstet Gynecol 2010;35:216-22.
8. Pina Pérez S, Jurado Seguer J, Pujadas AR, Serra Azuara L, Lleberia Juanos J, Aguiló Sagristà O. Role of intrapartum transperineal ultrasound: Angle of progression cut-off and correlation with delivery mode. Clin Obstet Gynecol Reprod Med 2017;3:1-4.
9. Tutschek B, Braun T, Chantraine F, Henrich W. A study of progress of labour using intrapartum translabial ultrasound, assessing head station, direction, and angle of descent. BJOG 2011;118:62-9.
10. Wiafe YA, Whitehead B, Venables H, Odoi AT. Sonographic parameters for diagnosing fetal head engagement during labour. Ultrasound 2018;26:16-21.
11. Kohls F, Brodowski L, Kuehnle E, Kniebusch N, Kalache KD, Weichert A. [Intrapartum Translabial Ultrasound: A Systematic Analysis of The Fetal Head Station in The First Stage of Labor]. Z Geburtshilfe Neonatol 2018;222:19-24.
12. Ionescu CA, Coroleucă C, Pleș L, Dimitriu M, Banacu M, Viezuină R, Bohiltea R. Ultrasound during labour. Gineco.eu 2016;12:211-3.
13. Henrich W, Dudenhausen J, Fuchs I, Kämena A, Tutschek B. Intrapartum translabial ultrasound (ITU): sonographic landmarks and correlation with successful vacuum extraction. Ultrasound Obstet Gynecol 2006;28:753-60.
14. Dückelmann AM, Bamberg C, Michaelis SAM, Lange J, Nonnenmacher A, Dudenhausen JW, et al. Measurement of fetal head descent using the 'angle of progression' on transperineal ultrasound imaging is reliable regardless of fetal head station or ultrasound expertise. Ultrasound Obstet Gynecol 2010;35:216-22.
15. Zilianti M, Azuaga A, Calderon F, Pagés G, Mendoza G. Monitoring the effacement of the uterine cervix by transperineal sonography: a new perspective. J Ultrasound Med 1995;14:719-24.
16. Sherer DM. Intrapartum ultrasound. Ultrasound Obstet Gynecol 2007;30:123-39.
17. Molina FS, Nicolaides KH. Ultrasound in labor and

delivery. Fetal Diagn Ther 2010;27:61-7.
18. Ahn KH, Oh M-J. Intrapartum ultrasound: A useful method for evaluating labor progress and predicting operative vaginal delivery. Obstet Gynecol Sci 2014;57:427.
19. Kalache KD, Dückelmann AM, Michaelis SAM, Lange J, Cichon G, Dudenhausen JW. Transperineal ultrasound imaging in prolonged second stage of labor with occipitoanterior presenting fetuses: how well does the "angle of progression" predict the mode of delivery? Ultrasound Obstet Gynecol 2009;33:326-30.
20. Barbera AF, Imani F, Becker T, Lezotte DC, Hobbins JC. Anatomic relationship between the pubic symphysis and ischial spines and its clinical significance in the assessment of fetal head engagement and station during labor. Ultrasound Obstet Gynecol 2009;33:320-5.
21. Bamberg C, Scheuermann S, Slowinski T, Dückelmann AM, Vogt M, Nguyen-Dobinsky TN, et al. Relationship between fetal head station established using an open magnetic resonance imaging scanner and the angle of progression determined by transperineal ultrasound. Ultrasound Obstet Gynecol 2011;37:712-6.
22. Usman S, Lees C. Benefits and pitfalls of the use of intrapartum ultrasound. Australas J Ultrasound Med 2015;18:53-9.
23. Levy R, Zaks S, Ben-Arie A, Perlman S, Hagay Z, Vaisbuch E. Can angle of progression in pregnant women before onset of labor predict mode of delivery? Ultrasound Obstet Gynecol 2012;40:332-7.
24. Gillor M, Vaisbuch E, Zaks S, Barak O, Hagay Z, Levy R. Transperineal sonographic assessment of angle of progression as a predictor of successful vaginal delivery following induction of labor. Ultrasound Obstet Gynecol 2017;49:240-5.
25. Minajagi PS, Srinivas SB, Hebbar S. Predicting the Mode of Delivery by Angle of Progression (AOP) before the Onset of Labor by Transperineal Ultrasound in Nulliparous Women. Curr Women's Health Rev 2020;16:39-45.
26. Eggebø TM, Hassan WA, Salvesen KÅ, Lindtjørn E, Lees CC. Sonographic prediction of vaginal delivery in prolonged labor: a two-center study. Ultrasound Obstet Gynecol 2014;43:195-201.
27. Torkildsen EA, Salvesen KÅ, Eggebø TM. Prediction of delivery mode with transperineal ultrasound in women with prolonged first stage of labor. Ultrasound Obstet Gynecol 2011;37:702-8.
28. Tan PC, Vallikkannu N, Suguna S, Quek KF, Hassan J. Transvaginal sonographic measurement of cervical length vs. Bishop score in labor induction at term: tolerability and prediction of Cesarean delivery. Ultrasound Obstet Gynecol 2007;29:568-73.
29. Giyahi H, Marsosi V, Faghihzadeh S, Kalbasi M, Lamyian M. Sonographic measurement of cervical length and its relation to the onset of spontaneous labour and the mode of delivery. Natl Med J India 2018;31:70.
30. Alanwar A, Hussein SH, Allam HA, Hussein AM, Abdelazim IA, Abbas AM, et al. Transvaginal sonographic measurement of cervical length versus Bishop score in labor induction at term for prediction of caesarean delivery. J Matern Neonatal Med 2019;1-8.
31. Verhoeven CJM, Opmeer BC, Oei SG, Latour V, van der Post JAM, Mol BWJ. Transvaginal sonographic assessment of cervical length and wedging for predicting outcome of labor induction at term: a systematic review and meta-analysis. Ultrasound Obstet Gynecol 2013;42:500-8.
32. Khazardoost S, Ghotbizadeh Vahdani F, Latifi S, Borna S, Tahani M, Rezaei MA, et al. Pre-induction translabial ultrasound measurements in predicting mode of delivery compared to bishop score: a cross-sectional study. BMC Pregnancy Childbirth 2016;16:330.
33. Aggarwal K, Yadav A. Role of transvaginal ultrasonographic cervical assessment in predicting the outcome of induction of labor. Int J Reprod Contraception Obstet Gynecol 2019;8:628.
34. Wiafe YA, Whitehead B, Venables H, Dassah ET. Comparing intrapartum ultrasound and clinical examination in the assessment of fetal head position in African women. J Ultrason 2019;19:249-54.
35. Eggebø TM, Hassan WA, Salvesen KÅ, Torkildsen EA, Østborg TB, Lees CC. Prediction of delivery mode by ultrasound-assessed fetal position in nulliparous women with prolonged first stage of labor. Ultrasound Obstet Gynecol 2015;46:606-10.
36. Choi SK, Park YG, Lee DH, Ko HS, Park IY, Shin JC. Sonographic assessment of fetal occiput position during labor for the prediction of labor dystocia and perinatal outcomes. J Matern Neonatal Med 2016;29:3988-92.
37. Akmal S, Kametas N, Tsoi E, Howard R, Nicolaides KH. Ultrasonographic occiput position in early labour in the prediction of caesarean section. BJOG 2004;111:532-6.
38. Verhoeven CJM, Rückert MEPF, Opmeer BC, Pajkrt E, Mol BWJ. Ultrasonographic fetal head position to predict mode of delivery: A systematic review and bivariate meta-analysis. Ultrasound Obstet Gynecol 2012;40:9-13.
39. Eggebø TM, Wilhelm-Benartzi C, Hassan WA, Usman S, Salvesen KA, Lees CC. A model to predict vaginal delivery in nulliparous women based on maternal characteristics and intrapartum ultrasound. Am J Obstet Gynecol 2015;213:362.e1-362.e6.

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OBSTETRICS

Risk Factors for Insulin Therapy in Gestational Diabetes Mellitus

Sriwipa Kaewsrinual, M.D.*,
Dittakarn Boriboonhirunsarn, M.D., M.P.H., Ph.D.*

** Department of Obstetrics and Gynaecology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand*

ABSTRACT

Objectives: To determine the factors associated with insulin requirement in patients with gestational diabetes mellitus (GDM) and compare the obstetrics outcomes between those who required insulin therapy and who did not.

Materials and Methods: A case-control study was conducted, including 100 GDM women who required insulin therapy as cases and 400 GDM women who did not require insulin therapy as controls. Data on baseline and obstetric characteristics, antenatal care, GDM risks, screening and diagnostic test results, labor and delivery, and obstetrics outcomes were reviewed from the medical records.

Results: Cases were significantly more likely to be nulliparous, overweight or obese, have DM in family, have had prior GDM, had higher number of GDM risks than controls. Compared with controls, cases had significantly higher plasma glucose level at fasting, 1, and 2 hours, but not at 3 hours after glucose loading and higher rate of abnormal fasting plasma glucose values and higher number of abnormal OGTT values. Logistic regression analysis showed that independent associated factors for insulin requirement were fasting plasma glucose (FPG) at OGTT > 95 mg/dL (adjusted odds ratio (OR) 20.8, 95% confidence interval (CI) 11.4-37.9), overweight or obesity (adjusted OR 1.9, 95%CI 1.1-3.5) and family history of DM (adjusted OR 2.2, 95%CI 1.2-3.9). While other pregnancy outcomes were comparable between the 2 groups, infants of cases were significantly more likely to have neonatal hypoglycemia and need for phototherapy.

Conclusion: Independent associated risks for insulin therapy in GDM women included FPG of > 95 mg/dL at OGTT, overweight or obesity, and family history of DM.

Keywords: gestational diabetes mellitus, insulin, risk factor, pregnancy outcomes.

Correspondence to: *Dittakarn Boriboonhirunsarn, M.D., M.P.H., Ph.D., Department of Obstetrics and Gynaecology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok 10700, Thailand. E-mail: dittakarn.bor@mahidol.ac.th*

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ปัจจัยเสี่ยงที่ทำให้ต้องใช้อินสุลินเพื่อควบคุมระดับน้ำตาลในมารดาที่เป็นเบาหวานขณะตั้งครรภ์

ศรีวิภา แก้วศรีนวล, ดิฐกานต์ บริบูรณ์หิรัญสาร

บทคัดย่อ

วัตถุประสงค์: *เพื่อศึกษาปัจจัยที่เกี่ยวข้องกับการต้องใช้อินสุลินเพื่อควบคุมระดับน้ำตาลในสตรีที่มีภาวะเบาหวานขณะตั้งครรภ์ และเปรียบเทียบผลลัพธ์ของการตั้งครรภ์ระหว่างสตรีที่มีภาวะเบาหวานขณะตั้งครรภ์ที่ใช้และไม่ใช้อินสุลิน*

วัสดุและวิธีการ: *ทำการศึกษาแบบ case-control โดยสตรีที่มีภาวะเบาหวานขณะตั้งครรภ์ที่ต้องใช้อินสุลิน จำนวน 100 คน เป็นกลุ่มศึกษา (case) และ สตรีที่มีภาวะเบาหวานขณะตั้งครรภ์ที่ไม่ต้องใช้อินสุลิน จำนวน 400 คน เป็นกลุ่มควบคุม (control) ทำการค้นข้อมูลจากเวชระเบียน ได้แก่ ข้อมูลพื้นฐานทั่วไป ข้อมูลทางสูติศาสตร์ การฝากครรภ์ ความเสี่ยงของภาวะเบาหวานระหว่างตั้งครรภ์ ผลการตรวจคัดกรองและวินิจฉัย การคลอด และผลลัพธ์ของการตั้งครรภ์*

ผลการศึกษา: *กลุ่มศึกษา เป็นสตรีที่คลอดครั้งแรก มีภาวะน้ำหนักเกินหรืออ้วน มีประวัติเบาหวานในครอบครัว เคยมีภาวะเบาหวานระหว่างตั้งครรภ์มาก่อน และมีจำนวนของปัจจัยเสี่ยง มากกว่ากลุ่มควบคุมอย่างมีนัยสำคัญทางสถิติ นอกจากนั้นเมื่อเทียบกับกลุ่มควบคุม กลุ่มศึกษามีค่าระดับน้ำตาลขณะอดอาหารและที่ 1 และ 2 ชั่วโมง หลังกินน้ำตาล ในการตรวจ 100-g Oral glucose tolerance test และมีอัตราความผิดปกติของระดับน้ำตาลขณะอดอาหาร และจำนวนของค่าที่ผิดปกติสูงกว่าอย่างมีนัยสำคัญทางสถิติ จากการวิเคราะห์แบบ logistic regression analysis พบว่าปัจจัยเสี่ยงที่สำคัญของการต้องใช้อินสุลิน ได้แก่ ค่าน้ำตาลหลังอดอาหารมากกว่า 95 มิลลิกรัมต่อเดซิลิตร (adjusted odds ratio (OR) 20.8, 95% confidence interval (CI) 11.4-37.9) ภาวะน้ำหนักเกินหรืออ้วน (adjusted OR 1.9, 95%CI 1.1-3.5) และประวัติโรคเบาหวานในครอบครัว (adjusted OR 2.2, 95%CI 1.3-3.9) ผลลัพธ์ของการตั้งครรภ์ส่วนใหญ่ ไม่มีความแตกต่างกันระหว่าง 2 กลุ่ม แต่พบว่าทารกของมารดากลุ่มศึกษา มีภาวะน้ำตาลต่ำ และภาวะตัวเหลืองที่ต้องส่องไฟรักษา สูงกว่าในกลุ่มควบคุมอย่างมีนัยสำคัญทางสถิติ*

สรุป: *ปัจจัยเสี่ยงที่สำคัญของการต้องใช้อินสุลินในสตรีตั้งครรภ์ที่มีภาวะเบาหวานระหว่างตั้งครรภ์ ได้แก่ ค่าน้ำตาลหลังอดอาหารมากกว่า 95 มิลลิกรัมต่อเดซิลิตร ภาวะน้ำหนักเกินหรืออ้วน และประวัติโรคเบาหวานในครอบครัว*

คำสำคัญ: *ภาวะเบาหวานระหว่างตั้งครรภ์ อินสุลิน ปัจจัยเสี่ยง ผลลัพธ์ของการตั้งครรภ์*

Introduction

Gestational diabetes mellitus (GDM) is one of the most common complications in pregnancy. Recent data shows that GDM prevalence has increased over time in association with the increase in prevalence of overweight or obesity in pregnant women[1, 2]. GDM has been associated with short and long-term consequences in both mother and the fetus, including preeclampsia, large for gestational age (LGA), macrosomia, shoulder dystocia, increased risk of caesarean section. In addition, GDM women have a greater risk of developing diabetes of mother and child in the future[3-5].

Initial management in GDM involves counseling, nutritional therapy, behavioral modification, and blood glucose control and monitoring[1, 2]. The goal of blood glucose level is fasting plasma glucose (FPG) of ≤ 95 mg/dL, 1-hour postprandial plasma glucose (1-hr PPG) of ≤ 140 mg/dL, and 2-hour postprandial plasma glucose (2-hr PPG) of ≤ 120 mg/dL. When these initial measures fail to control blood glucose in desirable range, additional pharmacological therapy is required, including various oral antidiabetic drugs and insulin[6-8]. However, insulin therapy is generally recommended as a first-line medication[1, 2, 6-8]. The rate of the need for insulin therapy varies between studies but it is estimated that, in general, approximately 10-20% of GDM women requires insulin therapy[1]. A recent study in Siriraj Hospital showed that insulin therapy was required in 12% of GDM women[9].

Inability to achieve glycemic control and prolonged hyperglycemia in GDM women has been associated with poor pregnancy outcomes, including preeclampsia, large-for-gestational-age (LGA), macrosomia, shoulder dystocia, operative delivery, birth trauma, neonatal hypoglycemia, hyperbilirubinemia, and hypocalcemia. However, early identification of GDM women who need insulin therapy and appropriate interventions could probably reduce such adverse maternal and neonatal outcomes as reported from previous studies[4, 5].

Several factors have been investigated and reported as the possible predicting factors for the need of insulin therapy in GDM women. These included high FPG level, the number of abnormal values of 100-g oral glucose tolerance test (OGTT), overweight or obesity, family history of diabetes mellitus, previous GDM, and early GDM diagnosis[9-15]. However, the results varied between studies, probably due to differences in population characteristics, screening and diagnostic strategies, management guidelines, and physician's preferences and decisions.

Currently, there is still limited information and research about this issue in the Siriraj Hospital. Therefore, this study was primarily aimed to determine factors associated with the need for insulin therapy among GDM women. In addition, pregnancy outcomes were compared between GDM women who required and did not require insulin therapy. Better understanding the associated risks could help predicting the need for insulin therapy among GDM women for better plan of more appropriate care and could help improving pregnancy outcomes.

Materials and Methods

After approval from Siriraj Institutional Review Board, a case-control study was conducted at the Department of Obstetrics and Gynecology, Faculty of Medicine, Siriraj Hospital. According to institutional guideline, GDM screening is offered to all at-risk pregnant women, using a 2-step approach. GDM risks include age > 30 years, pre-pregnancy BMI > 25 kg/m^2, family history of diabetes (DM in first-degree relatives), hypertension, previous GDM, history of fetal macrosomia, stillbirth, or fetal anomaly. A 50-g glucose challenge test (GCT) is used as a screening test at 140 mg/dL cut-off and a 100-g OGTT is used as a diagnostic test using Carpenter and Coustan criteria. The tests are offered at first antenatal visit and repeat during 24-28 weeks of gestation if the first tests are negative[16].

All women diagnosed with GDM initially received individual counseling regarding nutritional therapy and behavioral modification. Fasting and/or 2-hour PPG were used to monitor glycemic control

with the target of < 95 mg/dL and < 120 mg/dL, respectively, either by intermittent testing at each antenatal care visit or self-monitoring blood glucose (SMBG). Insulin therapy was offered if glycemic control within the target value was not achieved after nutritional and behavioral interventions, as appropriate. Generally, failure of nutritional intervention is considered when glycemic targets are not achieved in 3 consecutive antenatal care visits or there are > 70% abnormal glucose values from SMBG records. As of institutional guideline, no oral hypoglycemic agent was used. Management was offered by caring obstetricians and consultation with endocrinologists was done as appropriate.

Sample size was estimated based on the estimated rate of overweight and obesity of 50% and 33.3% among cases and controls. At 95% confidence level and 80% power with 4:1 control to case ratio, at least 90 cases and 360 controls were required. In this study, a total of 500 GDM women diagnosed according to institutional guideline were included. Exclusion criteria included pre-gestational diabetes, multiple pregnancy, fetal anomalies or fetal deaths, GDM diagnosed by other protocols, and GDM women who denied insulin therapy. Cases were 100 GDM women who required insulin therapy and controls were 400 GDM women who did not require insulin therapy. Both cases and controls were selected by simple random sampling procedure from pregnant women diagnosed with GDM.

Data was retrieved from medical records, including demographic data, antenatal care data, GDM risks, diagnosis, and screening and diagnostic test results, labor and delivery data, and pregnancy and neonatal outcomes. Pre-pregnancy body mass index (BMI) and gestational weight gain were classified according to the Institute of Medicine (IOM) recommendation[17].

Descriptive statistics, including mean, standard deviation, number, and percentage were used to describe various characteristics as appropriate. Student t-test and chi-square test or Fisher's exact test were used to compare various characteristics between cases and controls. Odds ratios (OR) and 95% confidence intervals (CI) were estimated to determine association between the need for insulin therapy and various characteristics. Logistic regression analysis was performed to evaluate independent associated factors for the need for insulin therapy, adjusted for potential confounders. A p value of < 0.05 was considered statistically significant. All analyses were performed using IBM SPSS Statistics for Windows®, Version 21.0. Armonk, NY: IBM Corp.

Results

A total of 100 cases of GDM women who required insulin therapy and 400 controls who did not need insulin therapy were included. Comparisons of baseline characteristics are shown in Table 1. Cases were more likely to be nulliparous (72% vs. 57.8%, p = 0.009). They had significantly higher BMI than controls (27.2 vs. 24.8 kg/m^2, p < 0.001) and they were significantly more likely to be overweight and obese (OR 3.9 and 3.5, respectively, p < 0.001). Comparison of GDM characteristics showed that GA at diagnosis and proportion of early-onset GDM were comparable. Regarding GDM risks, cases were significantly more likely to have DM in family, be overweight or obese, and have had prior GDM (OR 3.0, 3.6, and 4.9, respectively, p < 0.001). In addition, cases had significantly higher number of GDM risks (OR 2.5 for 2 risks, and 4.7 for > 3 risks, p < 0.001).

Comparison of plasma glucose levels from 100-g OGTT are shown in Table 2. Cases had significantly higher plasma glucose level at fasting, 1, and 2 hours, but not at 3 hours after glucose loading (p < 0.05). Compared with controls, cases were significantly more likely to have abnormal fasting plasma glucose values (81% vs. 13.3%, p < 0.001) while they were less likely to have abnormal 1- and 2-hour plasma glucose value (53% vs. 74.2%, p < 0.001, and 71% vs. 84%, p = 0.002, respectively) and comparable abnormal 3-hour value. Cases were significantly more likely to have higher number of abnormal OGTT values than controls (p < 0.001).

Table 1. Comparison of baseline characteristics between the 2 groups.

Characteristics	Controls N = 400	Cases N = 100	OR (95%CI)	p value
Mean age ± SD (years)	33.4 ± 5.2	32.6 ± 5.6		0.173
Mean BMI ± SD (kg/m^2)	24.8 ± 5.0	27.2 ± 5.2		< 0.001
Mean GA at diagnosis ± SD (weeks)	17.1 ± 9.2	15.5 ± 8.5		0.109
Nulliparous	231 (57.8%)	72 (72%)	1.9 (1.2-3.0)	0.009
BMI category				< 0.001
Normal	221 (55.3%)	26 (26%)		
Underweight	22 (5.5%)	4 (4%)	1.6 (0.5-4.8)	0.691
Overweight	99 (24.8%)	46 (46%)	3.9 (2.3-6.7)	< 0.001
Obese	58 (14.5%)	24 (24%)	3.5 (1.9-6.6)	< 0.001
Early-onset GDM (< 24 weeks)	260 (65%)	72 (72%)	1.4 (0.8-2.2)	0.185
GDM risks				
Age ≥ 30 years	315 (78.8%)	72 (72%)	0.7 (0.4-1.2)	0.149
Family history of DM	83 (20.8%)	44 (44%)	3.0 (1.9-4.8)	< 0.001
BMI ≥ 25 kg/m^2	157 (39.3%)	70 (70%)	3.6 (2.3-5.8)	< 0.001
Previous GDM	16 (4.0%)	17 (17%)	4.9 (2.4-10.1)	< 0.001
Previous fetal death	6 (1.5%)	2 (2%)	1.3 (0.3-6.7)	0.663
Previous macrosomia	6 (1.5%)	4 (4%)	2.7 (0.7-9.9)	0.119
Hypertension	40 (10%)	10 (10%)	1.0 (0.5-2.1)	1.00
Number of GDM risks				< 0.001
1 risk factor	219 (54.8%)	27 (27%)	1.0	
2 risk factors	121 (30.3%)	38 (38%)	2.5 (1.5-4.4)	< 0.001
≥ 3 risk factors	60 (15%)	35 (35%)	4.7 (2.7-8.4)	< 0.001

OR: odds ratio, CI: confidence intervals, SD: standard deviation, BMI: body mass index, GA: gestational age, DM: diabetes mellitus, GDM: gestational diabetes mellitus

Table 2. Comparison of baseline characteristics between the 2 groups.

Plasma glucose level of 100-g OGTT	Controls N = 400	Cases N = 100	p value
Mean fasting plasma glucose ± SD (mg/dL)	84.5 ± 13.0	126.0 ± 39.4	< 0.001
Mean 1-hour plasma glucose ± SD (mg/dL)	191.1 ± 26.3	216.8 ± 50.4	0.015
Mean 2-hour plasma glucose ± SD (mg/dL)	171.1 ± 21.2	197.2 ± 58.4	0.029
Mean 3-hour plasma glucose ± SD (mg/dL)	137.1 ± 27.5	155.3 ± 52.2	0.087
Abnormal plasma glucose values	N (%)	N (%)	
Fasting plasma glucose >95 mg/dL	53 (13.3)	81 (81)	< 0.001
1-hour plasma glucose >180 mg/dL	297 (74.3)	53 (53)	< 0.001
2-hour plasma glucose >155 mg/dL	336 (84)	71 (71)	0.002
3-hour plasma glucose >140 mg/dL	180 (45)	42 (42)	0.589
Number of abnormal values			< 0.001
Abnormal 2 values	153 (63.2)	55 (55)	
Abnormal 3 values	134 (33.5)	21 (21)	
Abnormal 4 values	13 (3.3)	24 (24)	

OGTT: oral glucose tolerance test, SD: standard deviation.

Pregnancy and neonatal outcomes were compared and the results are shown in Table 3. Maternal outcomes were comparable between cases and controls regarding gestational weight gain (GWG), GA at delivery, route of delivery, and preeclampsia. For neonatal outcomes, infants of cases were significantly more likely to have neonatal hypoglycemia and need for phototherapy. Both groups have comparable indications for cesarean section. Common indications for primary cesarean sections among cases and controls included cephalo-pelvic disproportion (23.6% vs. 25.7%), non-reassuring fetal heart rate (20.7% vs. 22.9%), and failed labor induction (9.3% vs. 11.4%).

Table 3. Comparison of pregnancy and neonatal outcomes between the 2 groups.

Outcomes	Controls N = 400	Cases N = 100	p value
Maternal outcomes			
Mean GWG ± SD (kg)	11.8 ± 5.3	11.2 ± 6.4	0.342
GWG category			0.514
Normal	142 (35.5%)	37 (37%)	
Inadequate	131 (32.8%)	27 (27%)	
Excessive	127 (31.8%)	36 (36%)	
Mean GA at delivery ± SD (weeks)	37.70 ± 1.78	37.53 ± 1.29	0.376
Route of delivery			0.835
Vaginal	182 (45.5%)	43 (43%)	
Primary C/S	140 (35%)	35 (35%)	
Repeat C/S	78 (19.5%)	22 (22%)	
Preeclampsia	62 (15.5%)	16 (16%)	0.902
Neonatal outcomes			
Mean birth weight ± SD (g)	3059.9 ± 525.8	3174.1 ± 577.9	0.058
Fetal LGA	102 (25.5%)	34 (34%)	0.088
Macrosomia	14 (3.5%)	7 (7%)	0.119
Apgar < 7 at 1 minute	22 (5.5%)	6 (6%)	0.846
Neonatal hypoglycemia	39 (9.8%)	17 (17%)	0.040
Phototherapy	80 (20%)	32 (32%)	0.010

GWG:, SD: standard deviation, GA: gestational age, C/S: cesarean section, LGA: large for gestational age.

Logistic regression analysis was performed to determine independent associated factors for the need of insulin therapy as shown in Table 4. After adjusted for age, parity, timing of GDM diagnosis, number of GDM risks, and number of abnormal OGTT values, independent associated risks for insulin therapy were FPG at OGTT > 95 mg/dL (adjusted OR 20.8, 95%CI 11.4-37.9, p < 0.001), overweight or obesity (adjusted OR 1.9, 95%CI 1.1-3.5, p = 0.029) and family history of DM (adjusted OR 2.2, 95%CI 1.2-3.9, p = 0.012).

Table 4. Logistic regression analysis to determine independent associated factors for insulin use, adjusted for potential confounders.

Factors	Adjusted OR	95% CI	p value
FPG at OGTT > 95 mg/dL	20.8	11.4 - 37.9	< 0.001
Overweight or obesity	1.9	1.1 - 3.5	0.029
Family history of DM	2.2	1.2 - 3.9	0.012

Adjusted for age, parity, timing of GDM diagnosis, number of GDM risks, and number of abnormal OGTT values

OR: odds ratio, CI: confidence intervals, FPG: fasting plasma glucose, OGTT: oral glucose tolerance test, DM: diabetes mellitus, GDM: gestational diabetes mellitus

Discussion

GDM women with poor glycemic control are associated with various adverse maternal and neonatal outcomes. Nutritional therapy and behavioral modification are commonly prescribed as initial treatment. However, when these measures fails, additional pharmacological treatment is needed for appropriate glycemic control and insulin is the first-line treatment of choice[1, 2, 6]. Identifying the factors related to the insulin requirement among GDM women is important in improving care process. This will help physician in identifying high-risk women who need close glycemic monitoring and can also aid in insulin treatment decision.

The results of this study showed that independent associated risks for insulin therapy were FPG of > 95 mg/dL at OGTT, overweight or obesity, and family history of DM. Abnormal FPG at the time of OGTT (> 95 mg/dL) showed the strongest association with adjusted OR of 20.8. Many previous studies have also reported that abnormal or high FPG level at the time of GDM diagnosis was related to the risk of insulin requirement[10, 11, 13-15]. A previous study reported that FPG of > 89.5 mg/dL had 72.7% sensitivity, 62.6% specificity, and 73% positive predictive value for insulin requirement[13]. While another study reported that FPG of >105 mg/dL at OGTT had a high specificity of 91.89% and positive predictive value of 80.64%[11].

Not only that overweight and obesity are among important risks for GDM[1, 2, 6, 16], they have been reported to be another significant risk for the need of insulin therapy similar to the results of this study[10, 12, 14]. A previous study in Siriraj Hospital also reported that overweight and obesity significantly increased the risk of insulin therapy as well[9]. Overweight and obese women might have higher degree of glucose intolerance and insulin resistance that increase the chance of nutritional therapy failure and consequently increase the risk for insulin therapy.

In this study, family history of DM also significantly increased the risk of insulin therapy among GDM women. A recent systematic review has reported that family history of DM was an important risk for development of GDM with odds ratio of 3.46[18]. In addition, another systematic review also reported that family history of DM significantly increased the risk of future type-2 DM as well[19]. Association between family history of DM and insulin requirement has been previously reported by a few previous studies[10, 12]. Genetic susceptibility for glucose intolerance and insulin resistance among women with family history of DM could have some roles in these observed results. However, exact underlying mechanism is still unknown and further studies regarding this specific issue are needed.

Many previous studies have reported association between HbA1c at the time of diagnosis and insulin therapy among GDM women[12, 13, 15, 20]. However, as HbA1c is not included as a routine test according to institutional guideline, such association could not be evaluated. Further studies might be required to determine if HbA1c is of value in predicting insulin requirement in GDM women. Other associated factors for insulin therapy that have been reported include maternal age, prior GDM[10], number of abnormal OGTT values[12], and gestational age at diagnosis[14]. These factors were also evaluated in this study but did not reach statistical significance level in multivariate analysis.

In terms of pregnancy outcomes, the results showed that infants of GDM women who required insulin therapy only increased the risk of neonatal hypoglycemia and the need for phototherapy, but not associated with other adverse outcomes. Awareness of both conditions, especially on neonatal hypoglycemia, should be raised when caring these infants after delivery. Previous studies have reported comparable pregnancy outcomes between the 2 groups that cesarean delivery, preterm birth, birth asphyxia, and NICU admission did not significantly increase with insulin therapy[11, 14]. However, increased birth weight and birth weight percentile have been reported[11]. Birth weight, LGA, and macrosomia only slightly higher in GDM women with insulin therapy, but without statistical significance. The absence of

significant association between some of the adverse pregnancy outcomes and insulin therapy may be partially due to the mitigating effects of GDM treatment.

Variations in the results between studies might be due to differences in population characteristics and risks, screening and diagnostic strategies, and management guidelines. While some studies used 75-g OGTT[13-15, 20], others used 100-g OGTT[9, 11, 12] for GDM diagnosis. Rates of insulin requirement in different settings also varied from 12% to 50% which partly reflects differences in population characteristics, risks and management scheme. However, some common risks were observed, e.g., high plasma glucose level at OGTT, pre-pregnancy overweight and obesity, etc., that might be useful to identify women at higher risk for insulin therapy.

The strengths of this study included the uniform screening and diagnosis and management guideline of GDM according to institutional guideline, and all GDM-related data were routinely recorded and collected systematically. Nonetheless, some deviations might exist from physicians' preference and judgment about insulin therapy. However, the issue should result only the delay in starting insulin and should not substantially alter the results. With regard to pregnancy outcomes, the study might have limited power to detect the differences between groups. In addition, effects of GDM treatments, both from nutritional and insulin therapy, on pregnancy outcomes could not be measured objectively. Further larger studies are needed to evaluate associated risks for insulin therapy as well as to determine if insulin therapy relates to adverse pregnancy outcomes in more details.

Nevertheless, the results of this study provide more insights on GDM management that are applicable into clinical practice. Understanding the significant risk factors will help caring physicians identify GDM women who are at higher risk for insulin therapy. Glycemic control of high-risk women should be closely monitored and decision on starting insulin therapy can be made in a timely manner. This might help GDM women to better achieve their glycemic target and minimize some related adverse pregnancy outcomes.

Conclusion

Independent associated risks for insulin therapy in GDM women included FPG of > 95 mg/dL at OGTT, overweight or obesity, and family history of DM. Infants of GDM women who required insulin therapy were significantly at higher risk of neonatal hypoglycemia and the need for phototherapy.

Potential conflicts of interest

The authors declare no conflict of interest.

References

1. American College of Obstetricians and Gynecologists. Committee on Practice Bulletins-Obstetrics. Practice Bulletin No. 190: Gestational diabetes mellitus. Obstet Gynecol 2018;131:e49-64.
2. American Diabetes Association. Standards of medical care in diabetes. Diabetes Care 2018;41(Suppl 1):S13-27.
3. Boriboonhirunsarn D, Talungjit P, Sunsaneevithayakul P, Sirisomboon R. Adverse pregnancy outcomes in gestational diabetes mellitus. J Med Assoc Thai 2006;89 Suppl 4:S23-8.
4. Crowther CA, Hiller JE, Moss JR, McPhee AJ, Jeffries WS, Robinson JS, et al. Effect of treatment of gestational diabetes mellitus on pregnancy outcomes. N Engl J Med 2005;352:2477-86.
5. Hartling L, Dryden DM, Guthrie A, Muise M, Vandermeer B, Donovan L. Benefits and harms of treating gestational diabetes mellitus: a systematic review and meta-analysis for the U.S. Preventive Services Task Force and the National Institutes of Health Office of Medical Applications of Research. Ann Intern Med 2013;159:123-9.
6. Szmuilowicz ED, Josefson JL, Metzger BE. Gestational Diabetes Mellitus. Endocrinol Metab Clin North Am 2019;48:479-93.
7. Mukerji G, Feig DS. Pharmacological Management of Gestational Diabetes Mellitus. Drugs 2017;77:1723-32.
8. Brown J, Grzeskowiak L, Williamson K, Downie MR, Crowther CA. Insulin for the treatment of women with gestational diabetes. Cochrane Database Syst Rev 2017;11:CD012037.
9. Ketumarn N, Boriboonhirunsarn D. Characteristics of abnormal oral glucose tolerance test in GDM diagnosis

and clinical correlation. J Matern Fetal Neonatal Med 2018;31:2109-14.
10. Souza A, Costa RA, Paganoti CF, Rodrigues AS, Zugaib M, Hadar E, et al. Can we stratify the risk for insulin need in women diagnosed early with gestational diabetes by fasting blood glucose? J Matern Fetal Neonatal Med 2019;32:2036-41.
11. Akinci B, Celtik A, Yener S, Yesil S. Is fasting glucose level during oral glucose tolerance test an indicator of the insulin need in gestational diabetes? Diabetes Res Clin Pract 2008;82:219-25.
12. Sapienza AD, Francisco RP, Trindade TC, Zugaib M. Factors predicting the need for insulin therapy in patients with gestational diabetes mellitus. Diabetes Res Clin Pract 2010;88:81-6.
13. Bakiner O, Bozkirli E, Ozsahin K, Sariturk C, Ertorer E. Risk Factors That can Predict Antenatal Insulin Need in Gestational Diabetes. J Clin Med Res 2013;5:381-8.
14. Wong VW, Jalaludin B. Gestational diabetes mellitus: who requires insulin therapy? Aust N Z J Obstet Gynaecol 2011;51:432-6.
15. Zhang Y, Shao J, Li F, Xu X. Factors in Gestational Diabetes Mellitus Predicting the Needs for Insulin Therapy. Int J Endocrinol 2016;2016:4858976.
16. Sunsaneevithayakul P, Boriboohirunsarn D, Sutanthavibul A, Ruangvutilert P, Kanokpongsakdi S, Singkiratana D, et al. Risk factor-based selective screening program for gestational diabetes mellitus in Siriraj Hospital: result from clinical practice guideline. J Med Assoc Thai 2003;86:708-14.
17. Rasmussen KM, Yaktine AL, editors. Weight gain during pregnancy: Reexamining the guidelines. Washington, DC: The National Academies Press; 2009.
18. Moosazadeh M, Asemi Z, Lankarani KB, Tabrizi R, Maharlouei N, Naghibzadeh-Tahami A, et al. Family history of diabetes and the risk of gestational diabetes mellitus in Iran: A systematic review and meta-analysis. Diabetes Metab Syndr 2017;11 Suppl 1:S99-S104.
19. Rayanagoudar G, Hashi AA, Zamora J, Khan KS, Hitman GA, Thangaratinam S. Quantification of the type 2 diabetes risk in women with gestational diabetes: a systematic review and meta-analysis of 95,750 women. Diabetologia 2016;59:1403-11.
20. Ducarme G, Desroys du Roure F, Grange J, Vital M, Le Thuaut A, Crespin-Delcourt I. Predictive factors of subsequent insulin requirement for glycemic control during pregnancy at diagnosis of gestational diabetes mellitus. Int J Gynaecol Obstet 2019;144:265-70.

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Survival Rate of Cervical Cancer Patients According to the 2018 FIGO Staging System: A tertiary hospital based study, Vajira Hospital, Bangkok

Pantana Bangsomboon, M.D.*,
Thannaporn Kittisiam, M.D.*,
Woraphot Chaowawanit, M.D.*

** Department of Obstetrics and Gynecology, Faculty of Medicine Vajira Hospital, Navamindradhiraj University, Bangkok, Thailand*

ABSTRACT

Objectives: To validate survival rate of cervical cancer patients based on the revised 2018 International Federation of Gynecology and Obstetrics (FIGO) staging system.

Materials and Methods: Medical records of cervical cancer patients from 2006-2015 were reviewed. The locally-advanced patients without radiological imaging or incomplete medical records were excluded. All included patients were assigned as FIGO 2018 staging criteria.

Results: Of the 226 patients with cervical cancer analyzed. Mean age was 51 ±12 years (17-90 years). Squamous cell carcinoma was the most common cell type in 159 patients (70.4%). According to FIGO 2018 staging criteria, 81 patients (35.8%) were upstaged. The 5-year progression-free survival (PFS) of stage IB1, IB2 and IB3 were 83.3%, 90.0% and 84.2%, respectively and the 5-year overall survivals (OS) were 71.4%, 92.2% and 62.5%, respectively. The PFS and OS were not different among 3 sub-stages. The 5-year PFS of stage IIIB, IIIC1 and IIIC2 were 68.6%, 89.3% and 62.5%, respectively and the 5-year OS were 71.4%, 92.2% and 62.5%, respectively. The PFS and OS of stage IIIB and IIIC2 were not significantly different ($p = 0.163$ and 0.166, respectively) while survival of stage IIIC1 was significantly higher than stage IIIB ($p = 0.025$ and 0.017, respectively) and IIIC1 ($p = 0.001$ and 0.001, respectively).

Conclusion: The revised 2018 FIGO staging system for cervical cancer was useful to distinguish survival rates of patients with locally-advanced disease and distant metastasis while the survival rate of sub-stages of early-stage disease was no different. Stage III disease, para-aortic metastasis was the most impact on the survival rate.

Keywords: FIGO 2018 staging, validation, cancer, cervix, survival rate.

Correspondence to: *Woraphot Chaowawanit, M.D., Department of Obstetrics and Gynecology, Faculty of Medicine Vajira Hospital, Navamindradhiraj University, Bangkok, Thailand. E-mail: woraphot@nmu.ac.th*

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อัตราการอยู่รอดของผู้ป่วยมะเร็งปากมดลูกตามการกำหนดระยะโรค 2018 FIGO staging system: การศึกษาในโรงพยาบาลตติยภูมิ, โรงพยาบาลวชิรพยาบาล กรุงเทพมหานคร

ภรรธนา บ่างสมบูรณ์, ธรรณพร กิตติสยาม, วรพจน์ เชาวะวณิช

บทคัดย่อ

วัตถุประสงค์: *เพื่อศึกษาอัตราการอยู่รอดของผู้ป่วยมะเร็งปากมดลูกตาม International Federation of Gynecology and Obstetrics 2018 staging system*

วัสดุและวิธีการ: *รวบรวมข้อมูลของผู้ป่วยมะเร็งปากมดลูกทั้งหมดที่มารักษาที่โรงพยาบาลวชิรพยาบาลระหว่างปี 2006-2015 จากฐานข้อมูล ผู้ป่วยที่นำมาวิเคราะห์ต้องมีภาพรังสีก่อนผ่าตัดหรือผลพยาธิเกี่ยวกับต่อมน้ำเหลือง*

ผลการศึกษา: *ผู้ป่วยมะเร็งปากมดลูก 226 ราย อายุเฉลี่ย 51±12 ปี เป็น Squamous cell carcinoma มากที่สุด 159 ราย หลังจากแบ่งระยะตาม FIGO 2018 staging พบมีระยะของโรคเพิ่มขึ้นจำนวน 81 ราย อัตราการรอดชีวิตโดยโรคสงบระยะ 5 ปี ของ IB1, IB2 and IB3 คือ ร้อยละ 83.3, 90.0 และ 84.2 อัตราการรอดชีวิตโดยรวม 5 ปี คือ ร้อยละ 71.4, 92.2 และ 62.5: ซึ่งไม่ต่างกัน อัตราการรอดชีวิตโดยโรคสงบระยะ 5 ปี ของ IIIB, IIIC1 และ IIIC2 คือ ร้อยละ 68.6, 89.3 และ 62.5 อัตราการรอดชีวิตโดยรวม 5 ปี คือ ร้อยละ 71.4, 92.2 และ 62.5 ตามลำดับ อัตราการรอดชีวิตโดยโรคสงบและอัตราการรอดชีวิตโดยรวมของ IIIB และ IIIC2 ไม่ต่างกัน (p = 0.163, 0.166) แต่ IIIC1 มากกว่า IIIB (p = 0.025, 0.017) และIIIC1 (p = 0.001, 0.001)*

สรุป: *FIGO2018 staging มีประโยชน์ในการบอกความแตกต่างของการอยู่รอดระหว่างระยะลุกลามเฉพาะที่และระยะแพร่กระจายในผู้ป่วยมะเร็งปากมดลูก ในขณะที่ระยะย่อยไม่สามารถบอกความแตกต่างได้ การลุกลามไปที่ต่อมน้ำเหลือง para-aortic มีผลต่ออัตราการอยู่รอดมากที่สุด*

คำสำคัญ: *FIGO 2018 staging, มะเร็ง, ปากมดลูก, อัตราการอยู่รอด*

Introduction

Cervical cancer is the fourth most common cancer in women worldwide. There was 569,847 new cases and 311,365 deaths in 2018. The majority of new cases and deaths occur in developing countries[1]. The International Federation of Gynecology and Obstetrics (FIGO) purposed the staging system for cervical cancer depending on pelvic examination and simple imaging studies[2] because the prevalence of cervical cancer is mainly in low-resourced areas including Thailand.

In 2018, the FIGO staging system was revised[3,4]. The new staging system allows the use of any imaging modality and/or pathological findings for determining the stage. However, some clinicians in low-resourced conditions can assess the patient clinically as before[4]. Table 1 shows the changes in FIGO staging system of cervical cancer between FIGO 2009[2] and 2018 staging system[3,4]. In stage IA, lateral extension has no longer been included. Stage IB is divided by tumor size into 3 sub-stages. Status of retroperitoneal lymph node is more concern in the new staging system. Metastatic lymph node on imaging or pathological studies is assigned stage IIIC (IIIC1 for only pelvic lymph node and IIIC2 for positive para-aortic lymph node) (Table 1).

Table 1. Changes in the FIGO staging system of cervical cancer.

Stage	2009 staging system	2018 staging system
IA1	Stromal invasion < 3 mm in depth and extension of ≤ 7 mm	Stromal invasion < 3 mm in depth
IA2	Stromal invasion > 3 mm and < 5 mm in depth and extension of ≤ 7 mm	Stromal invasion ≥ 3 mm and < 5 mm in depth
IB1	Tumor size ≤ 4 cm in greatest dimension	- Tumor size ≥ 5 mm depth of stromal invasion, and < 2 cm in greatest dimension - Positive margin of conization
IB2	Tumor size > 4 cm in greatest dimension	Tumor size ≥ 2 cm and < 4 cm in greatest dimension
IB3	N/A	Tumor size ≥ 4 cm in greatest dimension
IIA1	Tumor involve upper 2/3 of vagina and size ≤ 4 cm in greatest dimension	Tumor involve upper 2/3 of vagina and size < 4 cm in greatest dimension
IIA2	Tumor involve upper 2/3 of vagina and size > 4 cm in greatest dimension	Tumor involve upper 2/3 of vagina and size ≥ 4 cm in greatest dimension
IIIC1	N/A	Pelvic lymph node metastasis only*
IIIC2	N/A	Para-aortic lymph node metastasis*

* Either radiographic (r) or pathologic (p) studies confirmed metastasis
N/A, not available; FIGO, the International Federation of Gynecology and Obstetrics

The new staging system was validated by a retrospective study using The Surveillance, Epidemiology, and End Results (SEER) Program in the United States between 1988 and 2014[6]. The cause-specific survival is significantly difference among stage IB but survival in stage IIIC1 varies which it depends on the tumor size.

In Thailand, cervical cancer is the second most common cancer in women with 8,622 new cases and 5,015 deaths in 2018[5]. The 2009 FIGO

staging system had been applied for a past decade. Advance imaging modalities and minimally invasive surgery (MIS) are more available in some urban areas. The objective of this study was to determine the 5-year overall survivals (OS) and progression-free survival (PFS) according to the recent FIGO staging system.

Materials and Methods

After the ethics committee approval, medical records of all patients with cervical cancers from January 2006 to December 2015 were reviewed. The early-stage patients with pre-operative imaging (computerized tomography (CT) or magnetic resonance imaging (MRI)) or pathological study of pelvic and para-aortic lymph nodes were eligible. For the locally-advanced or distant disease, pre-treatment CT or MRI should be recorded. We excluded the patients with incomplete medical record. Patient characteristics, clinicopathologic data, treatment, disease outcomes and follow-up period were collected by review of medical records. All cases were defined the stage based on FIGO 2018 staging system[3,4].

All patients were treated based on 2009 FIGO staging system. For early-stage disease, extrafascial hysterectomy is a treatment for stage IA1 disease and radical hysterectomy with pelvic lymphadenectomy (RHPL) is a treatment for stage IA2, IB1 and IIA1 disease. Adjuvant concurrent chemoradiation (CCRT) or radiation after surgery are considered in high-risk patients including positive lymph node, positive surgical margin, positive parametrium, positive lymphovascular space invasion (LVSI), deep stromal invasion and large tumor size. For locally-advanced disease, CCRT is a treatment of choice. Palliative chemotherapy or best supportive care is introduced to stage IVB disease. After treatment completion, patients were followed-up every 3 months for the first 2 years, 6 months for 3-5 years, then annually. Palliative chemotherapy or pelvic radiation is a treatment option for recurrent disease.

All data were analyzed using SPSS statistical software, version 22.0. Descriptive statistics were used to analyze demographic data and were summarized as numbers with percentage or median with range. OS and PFS of the patients according to the prior and new stages were analyzed by the Kaplan-Meier method. The log-rank test was used to examine the statistical difference.

Table 2. Characteristics of 226 cervical cancer patients.

	N (%)
Mean age ± SD (years)	51.5 ± 12
Marital status	
- Single	70 (31.0)
- Married	119 (52.7)
- Divorced	17 (7.5)
- Widow	20 (8.8)
Histopathology	
- Squamous cell carcinoma	159 (70.4)
- Adenocarcinoma	56 (24.8)
- Adenosquamous carcinoma	1 (0.4)
- Neuroendocrine tumor	9 (4.0)
- Mixed cell types	1 (0.4)

SD: standard deviation

Results

From January 2006 and December 2015, 405 cervical cancer patients were identified. Seventeen women with incomplete medical records and 162 women without CT or MRI were excluded. The characteristics of 226 patients are summarized in Table 2. The mean age was 51.5 ± 12 years (range of 17-90 years). The most common cell type was squamous cell carcinoma (70.4%).

Based on the 2018 FIGO staging system, 81 patients (35.8%) were upstaged (Table 3). Twenty-eight early-stage patients were diagnosed as a higher stage because the cut-off tumor size had been changed. Of 46 women formerly staged as IB1 disease, 20 (43.5%) and 1 (2.2%) were upstaged to sub-stages IB2 and IB3, respectively. Of 7 patients formerly staged as IB2 disease, 4 (57.1%) were upstaged to sub-stages IB3. Of 44 patients staged as IIIC disease, 24 patients (54.5%) were assigned by CT or MRI and 20 patients (45.5%) were assigned by pathological finding. Thirteen patients (29.5%) were previously stage IB1 by 2009 staging system and 31 patients (71.5%) were previously locally-advanced disease (stage IB2, IIB, IIIA and IIIB).

Table 3. Numbers of patients staged by 2009 and 2018 staging criteria.

FIGO 2009	N (%)														
	IB1	**IB2**	**IB3**	**IIA1**	**IIA2**	**IIB**	**IIIA**	**IIIB**	**IIIC1r**	**IIIC1p**	**IIIC2r**	**IIIC2p**	**IVA**	**IVB**	**Total**
IA1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	1
IA2	1	-	-	-	-	-	-	-	-	-	-	-	-	-	1
IB1	10	20	1	-	-	2	-	-	1	11	-	1	-	-	46
IB2	-	-	4	-	-	-	-	-	-	3	-	-	-	-	7
IIA1	-	-	-	5	1	-	-	-	1	-	-	-	-	-	7
IIA2	-	-	-	-	1	-	-	-	-	-	-	-	-	-	1
IIB	-	-	-	-	-	36	-	-	5	2	3	1	-	2	49
IIIA	-	-	-	-	-	-	-	-	-	-	-	1	-	-	1
IIIB	-	-	-	-	-	-	-	35	5	-	9	1	2	3	55
IVA	-	-	-	-	-	-	-	-	-	-	-	-	24	-	24
IVB	-	-	-	-	-	-	-	-	-	-	-	-	-	34	34
Total	12	20	5	5	2	38	0	35	12	16	12	4	26	39	226

FIGO: the International Federation of Gynecology and Obstetrics

During 68 months of median follow-up time, there were 67 progression (29.6%) and 58 deaths (25.7%). Five-year PFS and OS of the 2009 and 2018 FIGO staging system are displayed in Table 4. For stage IB, the 5-year PFS and OS were not different between stage IB1 vs. IB2, IB2 vs. IB3 and IB1 vs. IB3 (Fig. 1A and 1B). The significant difference in PFS and OS was demonstrated in stage III (Fig. 1C and 1D). The 5-year PFS of stage IIIB, IIIC1 and IIIC2 were 68.6%, 89.3% and 62.5%, respectively and the 5-year OS were 71.4%, 92.2% and 62.5%, respectively, (Fig. 1C and 1D). The PFS and OS of stage IIIB and IIIC2 was not significantly different ($p = 0.163$ and 0.166, respectively).

Table 4. Five-year survival rate of 226 patients staged by 2009 and 2018 staging criteria.

	FIGO 2009 criteria			FIGO 2018 criteria		
	N (%)	5-yr PFS (%)	5-yr OS (%)	N (%)	5-yr PFS (%)	5-yr OS (%)
Stage I						
- IA1	1 (0.4)	100.0	100.0	-	-	-
- IA2	1 (0.4)	100.0	100.0	-	-	-
- IB1	46 (20.4)	84.8	91.3	12 (5.3)	83.3	91.7
- IB2	7 (3.1)	100.0	100.0	20 (8.8)	90.0	95.0
- IB3	-			5 (2.2)	100.0	100.0
Stage II						
- IIA1	7 (3.1)	85.7	100.0	5 (2.2)	80.0	100.0
- IIA2	1 (0.4)	0.0	0.0	2 (0.9)	50.0	50.0
- IIB	49 (21.7)	83.7	87.8	38 (16.8)	84.2	89.5
Stage III						
- IIIA	1 (0.4)	100.0	100.0	-	-	-
- IIIB	55 (24.3)	63.6	65.5	35 (15.5)	68.6	71.4
- IIIC1r	-	-	-	12 (5.3)	91.7	91.7
- IIIC1p	-	-	-	16 (7.1)	87.5	93.8
- IIIC2r	-	-	-	12 (5.3)	66.7	66.7
- IIIC2p	-	-	-	4 (1.8)	50.0	50.0
Stage IV						
- IVA	24 (10.6)	20.8	25	26 (11.5)	19.2	23.1
- IVB	34 (15.0)	2.9	2.9	39 (17.3)	5.1	5.1

FIGO: the International Federation of Gynecology and Obstetrics, PFS: progression-free survival, OS: overall survivals

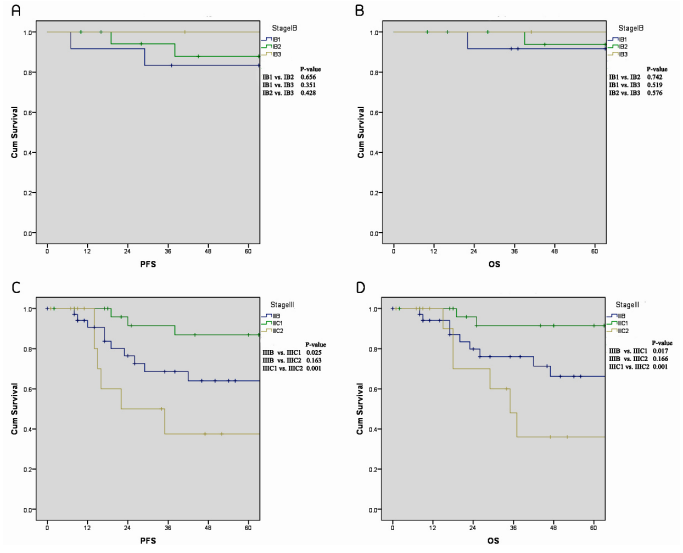

Fig. 1. (A) 5-year progression-free survival of stage IB1, IB2 and IB, (B) 5-year overall survival of stage IB1, IB2 and IB3, (C) 5-year progression-free survival of stage IIIB, IIIC1 and IIIC2, (D) 5-year overall survival of stage IIIB, IIIC1 and IIIC2.

Discussion

The 2018 FIGO staging system for cervical cancers allows any imaging modality and pathological assessment for tumor size, extension of tumor and metastatic retroperitoneal lymph nodes. The availability of advance imaging study has increased for last decade. Our study reported that 35.8% of all cases were upstaged by the revised criteria. Of 53 patients previously staged IB1 or IB2 disease, 25 patients (47.1%) were upstaged due to the change of the cut-off tumor size. For stage IB1 based on 2009 criteria, 20 patients (43.5%), 1 (2.2%), 12 (26.1%) and 1 (2.2%) were upstaged to sub-stages IB2, IB3, IIIC1 and IIIC2, respectively. For stage IB2, 4 patients (57.1%) and 3 (42.8%) were upstaged to sub-stages IB3 and IIIC1, respectively. The result of a retrospective study was similar to our study[7]. A total of 372 (87.5%) patients with stage IB1 or IB2 disease were assigned to a new staging system. Of 294 women formerly staged as IB1disease, 127 (43.2%), 29 (9.9%), 70 (23.8%), and 15 (5.1%) were upstaged to sub-stages IB2, IB3, IIIC1, and IIIC2, respectively. Of 131 patients formerly staged as IB2 disease, 66 (50.4%), 44 (33.6%), and 21 (16.0%) were upstaged to sub-stages IB3, IIIC1, and IIIC2, respectively[7].

On the literature review, the prevalence of stage IIIC1 was 25.9% and stage IIIC2 was 5.1%(8). In our cohort, the prevalence of stage IIIC1 was 12.4% and stage IIIC2 was 7.1%. The prevalence in our study was lower because 162 women without imaging were excluded. Our study revealed that 24 patients (54.5%) were assigned by CT or MRI and 20 patients (45.5%) were assigned by pathological finding. The sensitivity and specificity of imaging modalities to detect pelvic lymph node (PLN) and para-aortic lymph node (PALN) metastasis, had been reported in a retrospective study[9]. Yang et al found that that the sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of imaging modalities in detection of pelvic lymph node metastases were 88.9%, 22.2%, 69.6% and 50%, respectively, and 62.5%, 92%, 71.4% and 88.5%, respectively in para-aortic lymph node metastases[8]. The other retrospective data in Belgium studied 204 patients with locally-advanced cervical cancer with normal or not overtly PALN metastasis on imaging underwent surgical PALN staging[10]. Of 204 cases with negative imaging, PALN metastases were present in 8% at surgical staging[10].

In terms of survival outcome, two retrospective studies in United States validated the revised 2018 FIGO staging system[6,8]. For stage IB, 5-year survival rates were 94.6-97.0% for stage IB1 disease, 86.2-92.1% for stage IB2 disease, and 78.1-83.1% for stage 1B3 disease[6,8]. For stage III, 5-year survival rates were 46.0% for stage IIIA[6], 42.6% for stage IIIB[6], 61.9-62.1% for stage IIIC1 disease[6, 8], and 39.4% for stage IIIC2 disease[8], respectively. In subgroup analysis of stage IIIC, 5-year survival rate depended on tumor size and tumor extension (T-stage)[6,8]. Our results revealed that the difference among sub-stages of stage III disease was significantly while the difference among sub-stages of early-stage disease did not present.

Our institute is one of the tertiary hospitals in Bangkok. The survival outcomes of our patients may represent the survival rate of cervical cancer in urban area. The limitation of this study was the retrospective design. Additionally, the advance imaging modalities were not available in the past. Many cases were excluded because of incomplete medical records or unknown imaging studies. Presently, the CT or MRI are affordable in many hospitals, a prospective study may conduct. In order to achieve a larger population, co-operation of multicenter is necessary.

Conclusion

In conclusion, 35.8% of all cases were upstaged based on the revised 2018 FIGO staging system for cervical cancer. The advance imaging studies and staging surgery are important for allocating the stage. The new staging criteria were useful to distinguish survival rates of patients with locally-advanced disease and distant metastasis while the survival rate of sub-stages of early-stage disease was no different. Of stage III disease, para-aortic metastasis was the most impact

on the survival rate.

Acknowledgement

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Potential conflicts of interest

The authors declare no conflict of interest.

References

1. International Agency for Research on Cancer (2018). Population fact sheets [Internet]. 2018 [cited 2020 Aug 24]. Available from: https://gco.iarc.fr/
2. Pecorelli S. Revised FIGO staging for carcinoma of the vulva, cervix, and endometrium. Int J Gynaecol Obstet 2009;105:103-4.
3. Bhatla N, Aoki D, Sharma DN, Sankaranarayanan R. Cancer of the cervix uteri. Int J Gynaecol Obstet 2018;143 Suppl 2:22-36.
4. Bhatla N, Berek JS, Cuello Fredes M, Denny LA, Grenman S, Karunaratne K,et al. Revised FIGO staging for carcinoma of the cervix uteri. Int J Gynaecol Obstet 2019;145:129-35.
5. Matsuo K, Machida H, Mandelbaum RS, Konishi I, Mikami M. Validation of the 2018 FIGO cervical cancer staging system. Gynecol Oncol 2019;152:87-93.
6. Ayhan A, Aslan K, Bulut AN, Akilli H, Öz M, Haberal A, et al. Is the revised 2018 FIGO staging system for cervical cancer more prognostic than the 2009 FIGO staging system for women previously staged as IB disease? Eur J Obstet Gynecol Reprod Biol 2019;240:209-14.
7. McComas KN, Torgeson AM, Ager BJ, Hellekson C, Burt LM, Maurer KA, et al. The variable impact of positive lymph nodes in cervical cancer: Implications of the new FIGO staging system. Gynecol Oncol 2020;156:85-92.
8. Yang J, Delara R, Magrina J, Magtibay P, Yi J, Langstraat C, et al. Comparing survival outcomes between surgical and radiographic lymph node assessment in locally advanced cervical cancer: A propensity score-matched analysis. Gynecol Oncol 2020;156:320-7.
9. Vandeperre A, Van Limbergen E, Leunen K, Moerman P, Amant F, Vergote I. Para-aortic lymph node metastases in locally advanced cervical cancer: Comparison between surgical staging and imaging. Gynecol Oncol 2015;138:299-303.

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OBSTETRICS

Use of Placental Pulsatility Index in High Risk Pregnancy to Predict Fetal Growth Restriction

Natavadee Todumrong, M.D.*,
Dhirapatara Charoenvidhya, M.D.*,
Boonchai Uerpairojkit, M.D.*

** Department of Obstetrics and Gynecology, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand*

ABSTRACT

Objectives: The primary objective was to determine the predictive value of placental pulsatility index (PPI) in its ability to predict fetal growth restriction in singleton pregnant women at 16-24 weeks of gestation. The secondary objective was to evaluate PPI in predicting adverse perinatal outcomes and to compare the efficacy of PPI with conventional uterine artery pulsatility index (UtA PI) or umbilical artery pulsatility index (UA PI) alone.

Materials and Methods: A prospective observational study enrolled singleton pregnant women at 16- 24 weeks of gestation who were at high risk for fetal growth restriction and had prenatal care at the King Chulalongkorn Memorial Hospital between February 12, 2018, and January 28, 2019. UtA PI and UA PI were performed and calculated as PPI by transabdominal ultrasonography. Pregnancy outcomes were recorded. The optimal cut-off for PPI was derived from the receiver operating characteristic (ROC) curve to calculate the predictive values for fetal growth restriction.

Results: A total of 446 pregnant women were enrolled into the study. Twenty-seven cases (6%) developed fetal growth restriction. The optimal cut-off for PPI at 16-24 weeks of gestation was 1.38. The sensitivity, specificity, positive predictive value, and negative predictive value to predict fetal growth restriction were 66.7%, 78.8%, 16.8%, and 97.3%, respectively. The ROC curve of the PPI gave an area under the curve of 0.73 (95% CI,0.61-0.84).

Conclusion: In second-trimester high-risk pregnancies, PPI had a comparable performance in predicting FGR and adverse perinatal outcomes compared to UtA PI alone.

Keywords: placental pulsatility index, fetal growth restriction, adverse perinatal outcomes

Correspondence to: *Dhirapatara Charoenvidhya, M.D., Division of Maternal-Fetal Medicine, Department of Obstetrics and Gynecology, Faculty of Medicine, Chulalongkorn University, Bangkok 10330, Thailand*
E-mail: dhirapatara.c@chula.ac.th

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การใช้ Placental pulsatility index ในการทำนายภาวะทารกโตช้าในครรภ์ ในสตรีตั้งครรภ์ที่มีความเสี่ยงสูง

ณัฐวดี ต่อดำรงค์, ธีระภัทร เจริญวิทย์, บุญชัย เอื้อไพโรจน์กิจ

บทคัดย่อ

วัตถุประสงค์: *วัตถุประสงค์หลักเพื่อศึกษาหาค่าคาดทำนาย (Predictive value) จากการใช้ Placental pulsatility index (PPI) ในสตรีตั้งครรภ์เดี่ยวที่มีความเสี่ยงสูง อายุครรภ์ 16-24 สัปดาห์ ต่อการเกิดภาวะทารกโตช้าในครรภ์ วัตถุประสงห์รอง คือการใช้ Placental pulsatility index (PPI) ในสตรีตั้งครรภ์เดี่ยวที่มีความเสี่ยงสูง อายุครรภ์ 16-24 สัปดาห์ ในทำนายการเกิดภาวะแทรกซ้อนของทารกหลังคลอด และเปรียบเทียบประสิทธิภาพการทำนายภาวะทารกโตช้าในครรภ์ระหว่างการใช้ Placental pulsatility index (PPI) กับการใช้ Uterine artery-PI (UtA PI) หรือ umbilical artery-PI (UA PI) เพียงอย่างเดียว*

วัสดุและวิธีการ: *รูปแบบการศึกษาเป็นการศึกษาแบบไปข้างหน้าโดยทำการศึกษาในสตรีตั้งครรภ์เดี่ยวอายุครรภ์ 16-24 สัปดาห์มีความเสี่ยงสูงที่จะเกิดภาวะทารกโตช้าในครรภ์ที่มาฝากครรภ์ที่โรงพยาบาลจุฬาลงกรณ์ ระหว่างเดือนกุมภาพันธ์ 2561 ถึงเดือน มกราคม 2562 โดยได้ทำการตรวจคลื่นเสียงความถี่สูงทางหน้าท้องวัดค่า Uterine artery-PI (UtA PI) และ umbilical artery-PI (UA PI) และคำนวณค่า Placental pulsatility index (PPI) ทำการติดตามและบันทึกผลการคลอด วิเคราะห์หาค่าที่เหมาะสมของ Placental pulsatility index (PPI) จาก receiver operating characteristic (ROC) curve เพื่อทำนายภาวะทารกโตช้าในครรภ์*

ผลการศึกษา: *มีสตรีที่เข้าร่วมทำการวิจัยทั้งหมด 446 ราย มีทารกโตช้าในครรภ์ 27 ราย พบว่า PPI ที่มีค่า 1.38 สามารถนำมาใช้ทำนายการเกิดภาวะทารกโตช้าในครรภ์ได้ (sensitivity 66.7%, specificity 78.8%, PPV 16.8%, NPV 97.3%, ROC curve and 95%CI 0.73 (0.61-0.84))*

สรุป: *ในสตรีตั้งครรภ์เดี่ยวที่มีความเสี่ยงสูงจะเกิดภาวะทารกโตช้าในครรภ์การใช้ PPI ไม่ได้มีประสิทธิภาพของเหนือกว่าการใช้ UtA PI ในการทำนายภาวะทารกโตช้าในครรภ์และภาวะแทรกซ้อนของทารกหลังคลอด*

คำสำคัญ: *placental pulsatility index, ภาวะทารกโตช้าในครรภ์, ภาวะแทรกซ้อนของทารกหลังคลอด*

Introduction

Fetal growth restriction (FGR) is one of the most common conditions that increase the risk of perinatal complications. The short and long-term consequences of FGR are major public health problems, especially in developing countries[1,2]. This problem increased up to 40-50% in India and Mexico, and in Thailand, it was 10-20%[3]. This results in an untoward outcome and high medical costs.

The prediction of FGR has been a matter of concern for high-risk pregnancies and may be beneficial in lowering adverse perinatal outcomes. The use of a Doppler ultrasound is currently a valuable tool in predicting fetal well-being and perinatal outcome. There has been much research regarding uterine artery pulsatility index (UtA PI) and umbilical artery pulsatility index (UA PI) to predict FGR. However, its clinical use is still limited due to its low predictive performance[5,6].

Placental pulsatility index (PPI) is a ratio that combines vascular impedance of both fetal and maternal sides of the placenta. Doppler waveforms can increase the placental vascular impedance, which is related to FGR and are signs of impending fetal asphyxia.

Recently, Gudmudsson, et al[7] conducted a retrospective study on PPI, a new parameter that reflects the placental vascular impedance in predicting FGR in high-risk pregnancies during the third trimester of gestation. They found that PPI had a sensitivity, specificity, positive predictive value, and negative predictive value of 56%, 76%, 91%, and 30%, respectively, in predicting FGR[7]. So far, there is no prospective study using PPI to predict FGR in high-risk pregnancies at an earlier gestation. This prospective study assessed the efficacy of PPI in predicting FGR in high-risk pregnancies during the second trimester of gestation.

Materials and Methods

The research protocol was reviewed and approved by the ethics committee of the King Chulalongkorn Memorial Hospital (registered number 724/60). This prospective observational study was conducted at the King Chulalongkorn Memorial Hospital between February 2018 and January 2019. The eligible criteria were singleton pregnant women at 16 - 24 weeks of gestation and had at least 1 of the inclusion criteria. The inclusion criteria were advanced maternal age (≥ 35 years), previous history of pregnancy complications i.e., FGR, preterm, pregnancy-induced hypertension (PIH), gestational diabetes mellitus (GDM), stillbirth or perinatal death, preexisting medical illness such as chronic hypertension, diabetes mellitus, vascular disease, and renal impairment. The exclusion criteria were pregnant women who had fetal anomalies, fetal chromosomal abnormalities, morbid obesity (BMI ≥ 40), uterine anomalies, and those who refused to participate in the study. The gestational age (GA) was confirmed by ultrasonography during early gestation for all participants.

All participants with 16-24 weeks of gestation that met the inclusion criteria were enrolled in the study. UtA PI and UA PI measurements were performed on the same day by an experienced sonographer using the standard technique. Transabdominal ultrasonography (TAS) was obtained with 4 to 9 MHz IC5-9D (Voluson E10; GE Healthcare, Milwaukee, WI). UtA PI was performed on the lower lateral quadrants of the abdomen, angled medially. Color flow mapping was used to identify the UtA at the location where it crossed the external iliac artery. Pulsed wave Doppler was used to obtaining the UtA waveform by ensuring that the angle of the insonation was less than 30 degrees and at 1 cm downstream from this crossover point. UA PI was performed at a free loop, not too close to the fetus or the placental insertions. Three similar consecutive waveforms were obtained from UtA and UA[14]. PPI was calculated using this formula : PPI = (UA PI + mean of the left and the right Ut PI)/2[7]. The sample size was calculated using Gudmudsson S, et al.'s sensitivity of PPI to predict FGR (small for gestational age < 10 centiles)[7]. At the King Chulalongkorn Memorial Hospital, the incidence of FGR in all pregnancies was 5.9%[4]. Based on this calculation, the number of participants needed was 407. When 10% attrition rate of the follow-up participants was included in the

calculation, the total sample size was scaled up to 450 pregnant women.

Information on the study was provided to all participants by the research personnel. All participants received a copy of the study information. Signed informed consent was obtained from all participants after counseling. The participants were followed, and their data were collected after delivery. The data comprised of demographic characteristics, gestational age at TAS and delivery, results of UA and UtA Doppler parameters, placental weight, mode of delivery, indication for cesarean section, birth weight, APGAR score at 5 minutes, and perinatal outcomes.

The primary outcome was the efficacy of the PPI in predicting FGR in high-risk pregnancies. Secondary outcomes were comparisons of the efficacy of the PPI and conventional UtA PI or UA PI alone in predicting adverse perinatal outcomes.

Adverse perinatal outcomes included an APGAR score less than 7 at 5 minutes, respiratory distress syndrome (RDS), transient tachypnea of the newborn (TTNB), neonatal intensive care unit (NICU) admission within 48 hours, neonatal sepsis, intraventricular hemorrhage, pulmonary hemorrhage, hypothermia, hypoglycemia, bronchopulmonary dysplasia, necrotizing enterocolitis, perinatal death, and stillbirth.

Statistical analysis was performed using SPSS Version 22 (SPSS Inc., Chicago, Ill., USA). Descriptive statistics were presented as mean (SD) with a 95% confidence interval for continuous data and n (%) for categorical data. Analysis of continuous data was done by Student t-test, and categorical data were compared using Chi-square or Fischer exact test as appropriate. P-value of less than 0.05 was considered significant. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were assessed. Receiver operating characteristic (ROC) curves were constructed for PPI with FGR and adverse perinatal outcomes.

Results

Four hundred and fifty pregnant women were enrolled into this study. Four cases were excluded because one case had trisomy 21, one had major thalassemia, and the other two had fetal anomalies. After excluding those patients, the study was left with 446 pregnant women. The data from 446 participants were analyzed. Twenty-seven (6%) cases developed FGR.

The maternal characteristics are shown in Table 1. There were no statistically significant differences in age, the number of nulliparous, body mass index (BMI), GA at first ANC, and TAS between the FGR group and appropriate for gestational age (AGA) group. When the fetuses in the FGR group was compared to the AGA group, the FGR group had significantly higher number of preterm birth (33% vs 10.5%, $p < 0.001$), adverse perinatal outcomes (33% vs 7.4%, $p < 0.001$) and NICU admission (11.1% vs 2.6%, $p = 0.046$). They also had significantly lesser neonatal birth weight. However, there were no significant differences in the need for ventilator support, the number of fetuses with APGAR score less than 7 at 5 minutes and duration of hospital stay among the FGR group and the AGA group ($p > 0.05$) (Table 2.).

Table 1. Demographic characteristics of the women with and without FGR.

	AGA (n = 419)	FGR (n = 27)	p value
Maternal age (years)	35.8 (± 3.8)	35 (± 5.8)	0.260*
Nulliparous	150 (35.8)	11 (40.7)	0.604†
GA at first ANC (weeks)	9.5 (± 2.4)	10.6 (± 2.4)	0.513*
BMI at prepregnancy (kg/m^2)	22.8 (± 3.7)	22.2 (± 3.7)	0.409*
GA at USG (weeks)	18.8 (± 2)	19 (± 1.6)	0.669*

AGA: appropriate for gestational age, FGR: fetal growth restriction, GA: gestational age, ANC: antenatal care, BMI: Body mass index. † Chi-square test, * Student's T-test. Data are presented as n (%), and mean ± SD.

Table 2. Pregnancy outcomes of the women with and without FGR.

	AGA (n = 419)	FGR (n = 27)	p value
Birth weight (grams)	3,102 (± 432.4)	2,184 (± 588.4)	< 0.001*
GA at delivery (weeks)	38.3 (± 1.6)	36.9 (± 3.4)	< 0.001*
Preterm birth (< 37 weeks)	44 (10.5)	9 (33)	< 0.001†
Adverse perinatal outcome	31 (7.4)	9 (33)	< 0.001†
NICU admission	11 (2.6)	3 (11.1)	0.046‡
Need ventilator	10 (2.4)	1 (3.7)	0.501‡
APGAR score < 7 at 5 minutes	1 (0.2)	1 (3.7)	0.118‡
Duration of hospital stay (days)	4.6 (± 7.3)	4.9 (± 4.8)	0.833*

AGA: appropriate for gestational age, FGR: fetal growth restriction, GA: gestational age, NICU: Neonatal intensive care unit
† Chi-square test, ‡ Fisher's exact test, * Student's T-test. Data are presented as n (%), and mean ± SD

The ROC curve of PPI in predicting FGR gave an area under the curve of 0.73 (95% CI,0.61-0.84) with an optimal cut-off PPI of 1.38 (Fig. 1). This resulted in a sensitivity of 66.7%, a specificity of 78.8%, PPV of 16.8 %, and NPV of 97.3% for the prediction of FGR. UtA PI yielded a sensitivity of 59.3%, specificity of 87.1%, PPV of 22.9 % and NPV of 97.1% for the prediction of FGR (AUC = 0.75). UA PI yielded a sensitivity of 14.8%, a specificity of 88.8%, PPV of 7.8 %, and NPV of 94.2% for the prediction of FGR (AUC = 0.55) (Table 3).

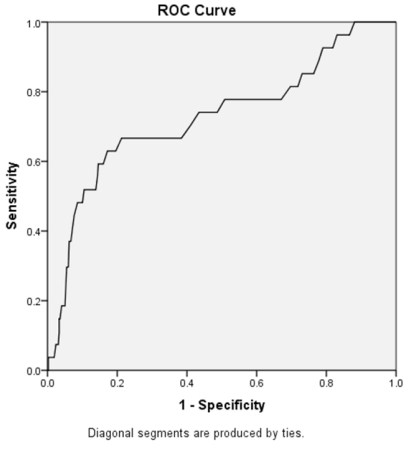

Fig. 1. Receiver operating characteristic curves of placental pulsatility index in predicting fetal growth restriction.

Table 3. Performance of PPI, UtA and UA doppler in predicting FGR.

	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)	ROC area and 95%CI
PPI > 1.38	66.7	78.8	16.8	97.3	0.73 (0.61-0.84)
Mean UtA PI > +2SD	59.3	87.1	22.9	97.1	0.75 (0.64-0.86)
Mean UA PI > +2SD	14.8	88.8	7.8	94.2	0.55 (0.44-0.66)

PPI: placental pulsatility index, UtA PI: uterine artery pulsatility index, UA PI: umbilical artery pulsatility index

As demonstrated in Table 4, PPI had a sensitivity of 47.4%, a specificity of 79.4%, PPV of 25.2 %, and NPV of 91.2% in predicting adverse perinatal outcomes. UtA PI had a sensitivity of 25%, a specificity of 85.2%, PPV of 14.9 %,

and NPV of 92% in predicting adverse perinatal outcomes. UA PI had a sensitivity of 10%, a specificity of 88.4%, PPV of 7.8 %, and NPV of 90.9% in predicting adverse perinatal outcomes. PPI had a higher sensitivity and PPV in predicting adverse perinatal outcomes compared to UtA PI or UA PI alone.

Table 4. Performance of PPI, UtA and UA doppler in predicting adverse perinatal outcomes.

	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)	ROC area and 95%CI
PPI > 1.38	47.4	79.4	25.2	91.2	0.63 (0.59-0.83)
Mean UtA PI > +2SD	59.3	87.1	22.9	97.1	0.75 (0.64-0.86)
Mean UA PI > +2SD	14.8	88.8	7.8	94.2	0.55 (0.44-0.66)

PPI: placental pulsatility index, UtA PI: uterine artery pulsatility index, UA PI: umbilical artery pulsatility index

The high PPI group had a significantly increased number of FGR, lower birth weight, and higher adverse perinatal outcomes compared to the normal PPI group ($p<0.001$). Nevertheless, the differences were not significant in GA at delivery, placental weight, number of fetuses with NICU admission, the need for ventilator support, number of fetuses with APGAR score less than 7 at 5 minutes, and duration of hospital stay as shown in Table 5.

Table 5. Comparison of pregnancy outcomes among high PPI group and normal PPI group.

	High PPI group (n = 107)	Normal PPI group (n = 339)	p value
GA at delivery (weeks)	37.9 (± 2.5)	38.3 (±1.5)	0.1*
Birth weight (grams)	2,861 (± 612.5)	3,105 (± 434.8)	< 0.001*
Placental weight (grams)	578 (± 126.5)	632 (± 129)	0.493*
FGR	18 (16.8)	9 (2.7)	< 0.001†
Adverse perinatal outcome	27 (25.2)	30 (8.8)	< 0.001†
NICU admission	6 (5.6)	8 (2.4)	0.093†
Need ventilator	4 (3.7)	7 (2.1)	0.331‡
APGAR score < 7 at 5 minutes	1 (0.9)	1 (0.3)	0.388‡
Duration of hospital stay (days)	5.4 (± 8.4)	4.3 (± 6.8)	0.179*

FGR: fetal growth restriction, GA: gestational age, NICU: Neonatal intensive care unit

† Chi-square test, ‡ Fisher's exact test, * Student's T-test. Data are presented as n (%), and mean ± SD

Discussion

FGR is a leading cause of perinatal morbidity and mortality. Currently, there is no screening strategy to predict FGR due to low predictive performances of the currently available tools. This indicates that there is a need to establish a more sensitive tool to predict FGR. Recently, Gudmudsson S, et al.'s[7] retrospective study reported that during the third trimester, PPI alone might improve the detection rate of FGR compared to either UtA PI or UA PI.

This prospective study of PPI is the first of its kind to predict FGR during the second trimester of high-risk pregnancies. The best cut-off value of PPI was 1.38 according to the ROC curve (ROC curve 0.73, 95% CI (0.61-0.84). At this cut-off value, the sensitivity (66.7%) and specificity (78.8%) to predict FGR were high. These results were consistent with the findings reported in Gudmundsson S, et al.'s study[7].

However, the PPV of PPI to predict FGR in our study was lower compared to Gudmundsson S, et al.'s

study[7]. This could be due to a low prevalence of FGR (6% (27/446)) in our study when compared to Gudmundsson S, et al.'s study, which had a prevalence of 80% (273/340). The higher PPV for FGR may not reflex a real clinical situation and can be due to selection bias. Their results may not be applicable in clinical practice. In addition, they screened for FGR in the third trimester, which may have a lesser clinical benefit when compared to our study which the screening was done at an earlier gestational period.

Our study showed that PPI had a higher sensitivity and higher PPV to predict adverse perinatal outcomes compared to UtA alone (sensitivity 47.4% vs 25%, specificity 79.4% vs 85.2%, PPV 25.2% vs 14.9%, NPV 91.2% vs 92%, ROC curve 0.63 vs 0.65, respectively).

In our study, the performance of UtA PI or UA PI alone to predict FGR was consistent with the results from previous studies[8, 15]. In contrast, Pongrojpaw D, et al.'s study[16] showed that the UtA PI had a lower prediction performance in predicting FGR and adverse perinatal outcomes.

The strength of this study was that we obtained PPI in high-risk pregnancies from the beginning and prospectively followed them until the FGR appeared. This conforms more to the context of screening and differs from the study that was performed retrospectively. In addition, the study was conducted in an earlier gestational period which may have a better clinical benefit in implementing an intervention to ameliorate the adverse clinical outcome.

Conclusion

In conclusion, in second-trimester high-risk pregnancies, PPI had a comparable performance in predicting FGR and adverse perinatal outcomes compared to UtA PI alone. Therefore, we recommend further study about PPI use combined with other serum markers to predict FGR and adverse perinatal outcomes.

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Potential conflicts of interest

The authors declare no conflict of interest.

References

1. ACOG Practice bulletin no. 134: fetal growth restriction. Obstet Gynecol 2013;121:1122-33.
2. Alfirevic Z, Stampalija T, Gyte GM. Fetal and umbilical Doppler ultrasound in normal pregnancy. Cochrane Database Syst Rev 2010; 4:CD001450.
3. Lee AC, Katz J, Blencowe H, Cousens S, Kozuki N, Vogel JP, et al; CHERG SGA-Preterm Birth Working Group. National and regional estimates of term and preterm babies born small for gestational age in 138 low-income and middle-income countries in 2010. Lancet Glob Health 2013;1:e26-36.
4. Patient statistics report from delivery room 2017, Department of Obstetrics - Gynecology, King Chulalongkorn Memorial Hospital.
5. Bower S, Schuchter K, Campbell S. Doppler ultrasound screening as part of routine antenatal scanning: prediction of pre-eclampsia and intrauterine growth retardation. Br J Obstet Gynaecol 1993;100:989-94.
6. De Paco C, Ventura W, Oliva R, Miguel M, Arteaga A, Nieto A, et al. Umbilical artery Doppler at 19 to 22 weeks of gestation in the prediction of adverse pregnancy outcomes. Prenat Diagn 2014;34:711-5.
7. Gudmundsson S, Flo K, Ghosh G, Wilsgaard T, Acharya G. Placental pulsatility index: a new, more sensitive parameter for predicting adverse outcome in pregnancies suspected of fetal growth restriction. Acta Obstet Gynecol Scand 2017;96:216-22.
8. Cnossen JS, Morris RK, ter Riet G, Mol BW, van der Post JA, Coomarasamy A, et al. Use of uterine artery Doppler ultrasonography to predict pre-eclampsia and intrauterine growth restriction: a systematic review and bivariable meta-analysis. CMAJ 2008;178:701-11.
9. Ghosh GS, Gudmundsson S. Uterine and umbilical artery Doppler are comparable in predicting perinatal outcome of growth-restricted fetuses. BJOG 2009;116:424-30.
10. Parra-Saavedra M, Crovetto F, Triunfo S, Savchev S, Peguero A, Nadal A, Gratacós E, Figueras F. Association of Doppler parameters with placental signs of underperfusion in late-onset small-for-gestational-age pregnancies. Ultrasound Obstet Gynecol 2014;44:330-7.

11. Li N, Ghosh G, Gudmundsson S. Uterine artery Doppler in high-risk pregnancies at 23-24 gestational weeks is of value in predicting adverse outcome of pregnancy and selecting cases for more intense surveillance. Acta Obstet Gynecol Scand 2014;93:1276-81.
12. García B, Llurba E, Valle L, Gómez-Roig MD, Juan M, Pérez-Matos C, et al. Do knowledge of uterine artery resistance in the second trimester and targeted surveillance improve maternal and perinatal outcome? UTOPIA study: a randomized controlled trial. Ultrasound Obstet Gynecol 2016;47:680-9.
13. Urbairojkit B. Fetal growth restriction. In : Charoenvidhya D, Urbairojkit B , Manotaya S, Tanawattanacharoen S, Panyakhamlerd K, editors. Obstretrics.3rd edition. Bangkok:O. S. Printing House 2005:341-50.
14. Bhide A, Acharya G, Bilardo CM, Brezinka C, Cafici D, Hernandez-Andrade E, et al. ISUOG practice guidelines: use of Doppler ultrasonography in obstetrics. Ultrasound Obstet Gynecol 2013;41:233-9.
15. Nagar T, Sharma D, Choudhary M, Khoiwal S, Nagar RP, Pandita A. The Role of Uterine and Umbilical Arterial Doppler in High-risk Pregnancy: A Prospective Observational Study from India. Clin Med Insights Reprod Health 2015;9:1-5.
16. Pongrojpaw D, Chanthasenanont A, Nanthakomon T. Second trimester uterine artery Doppler screening in prediction of adverse pregnancy outcome in high risk women. J Med Assoc Thai 2010;93 Suppl 7:S127-30.