48th Global Congress on MIGS
November 9-13 Vancouver, B.C., Canada

SYLLABUS

PLENARY 2:
Basic Science/Research/Education

Be a Surgical “Multiplier” in MIGS
Inspire Brilliance Through Teamwork
Professional Education Information

Target Audience
This educational activity is developed to meet the needs of surgical gynecologists in practice and in training, as well as other healthcare professionals in the field of gynecology.

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For more information or to view the policy please go to:
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Plenary 2: Basic Science/Research/Education

Moderator: Timothy B. McKinney, Sangeeta Senapati

Description
This session provides innovative techniques in laparoscopic gynecologic surgery, new teaching models for difficult clinical tasks, and large-scale data analyses related to trends in gynecologic surgery. Participants will be exposed to a broad range of study designs and research methodologies, including randomized trials, survey-based descriptive studies, and teaching videos.

Objectives
Learning Objectives: At the conclusion of this activity, the participant will be able to: 1) Discuss the broad range of study designs and research methodologies.

2:00  Differentially Expressed Genes in the Endometrium of Women with Intrauterine Adhesions
Discussant: A. Lin
L.V. Adamyan

2:10  Porcine Tongue Hysteroscopy: A Novel Simulation Model for Operative Hysteroscopy Teaching
Discussant: S. Khalil
E. Wright

2:20  Laparoscopic and Robotic Hysterectomy in Endometrial Cancer Patients with Obesity: A Systematic Review and Meta-Analysis of Conversions and Complications
Discussant: D.D. Namaky
M.C. Cusimano

2:30  Hysteroscopic Resection of a Complete Uterine and Vaginal Septum under Laparoscopic Ultrasound Guidance
Discussant: S.C. Tsai
H. Wirth

2:40  Gene Expression Signature in Diagnosis of Endometriosis
Discussant: J.E. Ocampo
Y.B. Aznaurova

2:50  Effect of Length of Surgery on the Incidence of Venous Thromboembolism after Benign Hysterectomy
Discussant: M. Bedaiwy
J.K. Moulder
PLANNER DISCLOSURE
The following members of AAGL have been involved in the educational planning of this workshop (listed in alphabetical order by last name).
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Linda D. Bradley, Medical Director, AAGL*
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Speakers Bureau: Laborie Medical Technologies, Teleflex Medical
Other: Unrestricted educational grant to support NC FPMRS Fellow Cadaver Lab: Boston Scientific Corp. Inc.
Amy Park*
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Harold Y. Wu*
Linda C. Yang
Other: Ownership Interest: KLAAS LLC

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The following have agreed to provide verbal disclosure of their relationships prior to their presentations. They have also agreed to support their presentations and clinical recommendations with the “best available evidence” from medical literature (in alphabetical order by last name).
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Yana B. Aznaurova*
Mohamed A. Bedaiwy
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Maria C. Cusimano*
Susan Khalil*
Alexander Lin*
Consultant: Laborie Inc., Reddress
Janelle K. Moulder
Consultant: Hologic
Devin D. Namaky*
Jaime E. Ocampo*
Sangeeta Senapati
Consultant: Allergan, Olympus
Other: Partner/Investor: KLAAS
Susan C. Tsai
Consultant: Boston Scientific, CVS caremark, GlaxoSmithKline
Speakers Bureau: Boehringer Ingelheim
Hannah Wirth*
Emily Wright*

Content Reviewer has nothing to disclose.

Asterisk (*) denotes no financial relationships to disclose.

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Linda Michels, Executive Director, AAGL*
Differentially expressed genes in the endometrium of women with intrauterine adhesions

Leila V. Adamyan MD, professor, academician of RAS

Disclosure

I have no financial relationships to disclose

Objective

After the conclusion of this presentation, the participants will be able to recognize that increased expression of studied genes may be involved in pathogenesis of IUA.

• Intrauterine adhesions is a pathology of the endometrium in which there is a violation of the anatomical integrity of the uterine cavity of variable severity (1).
• Globally, the incidence of IUA is increasing and ranges from 0.3 to 21.5% (1, 2).
• Despite the many options for treatment and prevention the recurrence rate of IUA remains high.

• Rates of recurrence after surgery are higher for moderate to severe intrauterine adhesions, (23%) and (62%) (3).
• Although IUA has been known for many years we still lack reliable methods of prevention of synechiae recurrence after surgical treatment (3).
• More studies are needed to better understand the pathogenesis of the disease.

MicroRNA (miRNA) are small, noncoding RNAs, 18 to 25 nucleotides in length, which are generally believed to either block the translation or induce the degradation of their target messenger RNAs (mRNAs), depending on the degree to which the miRNA and its target complement each other. It is evident that miRNA-mediated posttranscriptional gene regulation is vital in modulating aspects of the wound healing process, inflammation, angiogenesis, fibroblast repair, apoptosis, and expression or function of extracellular matrix (ECM), including IUA (5).

In the literature available to us in IUA no studies of candidate genes for pathophysiological changes occurring in the endometrium have been conducted.
Knowledge: identify of molecular genetic markers in endometrial tissue of women of reproductive age with intrauterine adhesions compared to endometrium of healthy women.

Comprehension: picture graphically

Increased expression of genes S100A8, HBB, VNN2, RGS2, ERAP2, AQP9, MNDA, TUBA3E, FSGR3B involved in the processes of fibrosis, apoptosis, immune response and inflammation, indicates the role of these processes in the pathogenesis of IUA.

<table>
<thead>
<tr>
<th>Gene Symbol</th>
<th>Description</th>
<th>Degree of Change</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>S100A8</td>
<td>S100 calcium binding protein A8</td>
<td>X 10.94</td>
<td>0.000443</td>
</tr>
<tr>
<td>HBB</td>
<td>hemoglobin, beta</td>
<td>X 5.53</td>
<td>0.020497</td>
</tr>
<tr>
<td>VNN2</td>
<td>vanin 2</td>
<td>X 5.1</td>
<td>0.004938</td>
</tr>
<tr>
<td>RGS2</td>
<td>regulator of G-protein signaling 2, 24kDa</td>
<td>X 4.97</td>
<td>0.007148</td>
</tr>
<tr>
<td>ERAP2</td>
<td>endoplasmic reticulum aminopeptidase 2</td>
<td>X 4.69</td>
<td>0.008723</td>
</tr>
<tr>
<td>AQP9</td>
<td>aquaporin 9</td>
<td>X 4.67</td>
<td>0.000299</td>
</tr>
<tr>
<td>MNDA</td>
<td>myeloid cell nuclear differentiation antigen</td>
<td>X 3.81</td>
<td>0.001250</td>
</tr>
<tr>
<td>TUBA3E</td>
<td>tubulin, alpha 3e; tubulin, alpha 3d; tubulin, alpha 3c</td>
<td>X 3.58</td>
<td>0.016996</td>
</tr>
<tr>
<td>FCGR3B</td>
<td>Fc fragment of IgG, low affinity IIIb, receptor (CD16b)</td>
<td>X 3.03</td>
<td>0.000820</td>
</tr>
</tbody>
</table>

Bio-informatics analysis of transcriptome analysis data

| Immune response (GO:0006955) | MNDA, FCGR3B, S100A8, HBB, ERAP2, AQP9 |
| Secretion (GO:0046903)        | MNDA, FCGR3B, S100A8, HBB, AQP9 |
| Cellular response to stimulus (GO:0007176) | MNDA, S100A8, HBB, ERAP2, AQP9 |
| Activation of neutrophils involved in the immune response (GO:0002283) | MNDA, FCGR3B, S100A8, HBB |
| Exocytosis (GO:0006887)       | MNDA, FCGR3B, S100A8, HBB |

Application: Dept. of Operative Gynecology of the National Medical Research Centre for Obst., Gyn. & Perinatology, Moscow.

Analysis: group 1 – patients with intrauterine adhesions (n=10), group 2 – healthy women without intrauterine adhesions (n=10) underwent surgical treatment in our hospital between September 2015 to December 2016.

Synthesis: Endometrial tissue samples were taken with a pipel biopsy in preoperative period followed by microarray expression profiling using GeneChip Human Exon 1.0 ST Arrays (Affymetrix, USA). Hysteroscopy was performed in the proliferative phase of the menstrual cycle; assessment of the severity of the disease was carried out based on the AFS classification (1988).

Evaluation: 10 genes were revealed to have at least 3-fold mRNA change in endometrial tissues of women with intrauterine adhesions compared to the endometrial tissues of women of group of conditionally healthy women, of which 9 genes show increased expression on case of intrauterine adhesions (S100A8, HBB, VNN2, RGS2, ERAP2, AQP9, MNDA, TUBA3E, FCGR3B) and 1 – decreased expression (NTRK3).

Summary: differences in gene expression levels in endometrial tissues of women with intrauterine adhesions may be helpful in a study of the pathogenesis of the lesion or used to design a molecular diagnostic tool suitable to individualize the treatment of the lesion.

• Our findings using bioinformatic analysis suggest that one of the causes of intrauterine adhesions is a deviation in the course of intercellular interaction in such patients. Perhaps this may be due to intrauterine infection the response to which leads to the development of adhesions.

• It can also be assumed that patients with IUA have different parameters of fine-tuning of the endometrial/uterine immune system as compared with women without IUA. Such difference in itself or enhanced by the background of intrauterine infection or endometrial trauma leads to a pathological process.

This results demonstrate that mRNAs may change the function of extracellular matrix by regulating their target genes and so, they may have important role in the molecular pathogenesis of IUA.

It should be noted that the analysis of differences in the representation of transcripts in the course of this work was carried out for small number of samples. More studies are also required to verify the roles of genes and the relevant signaling pathways in the pathophysiology of IUA.
Acknowledgments

Sergey Aleksandrovich Martynov, MD, Leading Researcher of gynecological department, Academician V.I. Kulakov National Medical Research Center of Obstetrics, Gynecology and Perinatology of the Ministry of Health of the Russian Federation; Moscow, Russian Federation.

Pamatit Magomedovna Khirieva, young researcher, obstetrician-gynecologist, applicant of gynecological department, Academician V.I. Kulakov National Medical Research Center of Obstetrics, Gynecology and Perinatology of the Ministry of Health of the Russian Federation; Moscow, Russian Federation.

Maria Vladimirovna Kuznetsova, PhD, Researcher of the laboratory of molecular genetics methods, Academician V.I. Kulakov National Medical Research Center of Obstetrics, Gynecology and Perinatology of the Ministry of Health of the Russian Federation; Moscow, Russian Federation.

Andrey Aleksandrovich Bystritskiy, PhD, Leading Researcher of the laboratory of molecular genetics methods, Academician V.I. Kulakov National Medical Research Center of Obstetrics, Gynecology and Perinatology of the Ministry of Health of the Russian Federation; Moscow, Russian Federation.

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Assia Arnoldovna Stepanian, MD, Academic of Women’s Health and Endoscopic Surgery; Atlanta, GA

References

Porcine Tongue Hysteroscopy: A Novel Simulation Model for Operative Hysteroscopy Teaching

Presenter: Emily Wright, MD
OBGYN, University of British Columbia
Vancouver, BC, Canada

Video Objective: Hysteroscopic surgery is a fundamental skill for all obstetricians and gynaecologists. Time pressure within each case and inadequate OR exposure times can limit hands-on skills acquisition for residents. In order to ensure residents are obtaining and practicing fundamental skills, it is essential to develop teaching methods that can be used outside of an OR setting. The porcine tongue model is a simple and inexpensive model for operative hysteroscopy teaching that is both realistic and effective in teaching residents the fundamentals of hysteroscopic surgery. This presentation outlines the assembly of the model, as well as shows real-time use of the model for teaching.

Setting: N/A

Interventions: N/A

Conclusion: The porcine tongue hysteroscopy model is a simple and effective simulation model for teaching residents the fundamentals of hysteroscopic surgery.
Laparoscopic and robotic hysterectomy in endometrial cancer patients with obesity: A systematic review and meta-analysis of conversions and complications

Dr. Maria Cusimano, MD PhD(c)
Department of Obstetrics & Gynaecology
University of Toronto

Disclosure

• I have no financial relationships to disclose.

Objectives

• Summarize the evidence on laparoscopic and robotic hysterectomy in endometrial cancer patients with obesity
• Quote evidence-based pooled estimates of the risks of conversion to laparotomy and other common complications when consenting patients with obesity for hysterectomy

65% of endometrial cancer patients have concurrent obesity or morbid obesity, and these rates are rising

Total laparoscopic hysterectomy (LH) may be underutilized or unsuccessful in this population

Robotic hysterectomy (RH) is an alternative, but is costly and existing reviews of normal weight or overweight cohorts show no benefit

To evaluate rates of conversion to laparotomy and perioperative complications with LH or RH, specifically in endometrial cancer patients with obesity (BMI ≥30kg/m²)

Search Strategy

- Dates: January 1, 2000 to July 18, 2018
- Databases: MEDLINE, EMBASE, EBM Reviews
- Hand Search: Previous reviews & clinical guidelines

Inclusion Criteria

- Population: EC patients with obesity (N>20)
- Intervention: LH or RH; +/- lymphadenectomy
- Outcomes: Conversion, injury, transfusion, VTE
- Study Type: RCT or cohort

Statistical Analysis

- Pooled proportions
- Generalized linear random/mixed-effects model & exact likelihood approach based on a binomial distribution

Risk of Bias Assessment

- Double-Arm: Newcastle Ottawa Scale
- Single-Arm: IHE Quality Appraisal Checklist
- Publication Bias: Funnel plots of conversions
Conclusions

- RH and LH have similar rates of perioperative complications in endometrial cancer patients with obesity (BMI ≥ 30).
- RH may reduce conversions due to positional intolerance in patients with morbid obesity (BMI ≥ 40).
- Existing literature is limited by selection and confounding bias; RCTs are needed to inform practice standards in this population.

Acknowledgements

- Dr. Andrea N. Simpson, MD MSc
- Dr. Fahima Dossa, MD PhD(c)
- Valentina Liani, BSc
- Yuvreet Kaur, BSc
- Dr. Sergio A. Arcuna, MD PhD
- Dr. Deborah Robertson, MD MSc
- Dr. Abheha Satkunaratnam, MD
- Dr. Marcus Q. Bernardini, MD MSc
- Dr. Sarah E. Ferguson, MD
- Dr. Nancy N. Baxter, MD PhD
References

Hysteroscopic Resection of a Complete Uterine and Vaginal Septum Under Laparoscopic Ultrasound Guidance

Presenter: Hannah Wirth, MD, MS
OBGYN, Kaiser Permanente Los Angeles Medical Center
Los Angeles, CA

Video Objective: The aim of this video is to demonstrate the use of laparoscopic ultrasound guidance during hysteroscopic resection of a congenital uterine and vaginal septum.

Setting: Our patient is a 20 year old G0 female who presented for difficulty with tampon insertion and removal as well as painful intercourse. On physical exam, the patient was noted to have a complete, non-obstructing longitudinal vaginal septum with two separate normal cervices. MRI of the abdomen and pelvis showed a complete septate uterus, two cervices, and two normal kidneys.

Interventions: This video shows the simultaneous use of hysteroscopy and laparoscopic ultrasound to safely and successfully resect the uterine and vaginal septum.

Conclusion: The goal is to encourage use of this technique during similar procedures for patients with mullerian duct anomalies desiring surgical correction.
Objectives
Discuss the features of molecular signature of endometrial samples from women with and without endometriosis and its potential role in early diagnosis.

Endometriosis
Endometriosis – one of the most enigmatic gynecological disease. It is associated with chronic pelvic pain, dyspareunia, dysmenorrhea and in 30% of cases might cause infertility.

The gold standard for the diagnosis of endometriosis – laparoscopy with histological confirmation.

There are no effective and specific biomarkers of endometriosis in the blood, urine or saliva.

It is necessary to develop new minimally invasive methods for the diagnosis of endometriosis and for monitoring the effectiveness of treatment.

Eutopic and ectopic endometrium
- Previously, many scientists have shown that eutopic and ectopic endometrium are morphologically similar
- But it is very difficult to create diagnostic test based on these characteristics.
- That is why it is relevant to look for biomarkers at deeper levels of regulation - genomic and transcriptomic levels.

Update on biomarkers
- Research is in transition from the existing technologies (one gene, one mutation) to the large-scale analysis of gene expression and analysis of the activation of intracellular signaling pathways.
- Understanding how signaling pathways are activated allows us to indicate what processes in diseased cells are altered at the molecular level.

The degree of signaling pathways activation is more stable and reliable marker for some diseases than individual gene expression (Borisov et al, 2014).

Disclosure
“I have no financial relationships to disclose”
Signaling pathways

Signaling pathway is a cascade of protein-protein interactions, responsible for signal transferring from the receptor into the cell.

- the signal is transferred from molecule to molecule in a strictly defined sequence;
- signaling pathways activate in response to neurotransmitters, hormones, and growth factors;
- each signaling pathway is responsible for a particular cellular process.

Study design

The main goal is to identify all specific changes at the gene expression level and changes of intracellular signaling pathways activity in eutopic endometrium and endometriotic samples (ectopic endometrium) of patients with endometriosis.

Inclusion criteria:

- reproductive age
- absence of any hormone therapy over 1 year prior to surgery
- absence of other diseases of the uterus, fallopian tubes, and ovaries

Control group:

- women with uterine scar incompetence after cesarean section.

Results

We profiled 52 endometrial pathological samples and 12 corresponding normal endometrium by RNA sequencing. We performed two-step differential gene analysis of endometrial samples and endometriotic lesions of patients with endometriosis in comparison with healthy endometrium. Based on this analysis we generated a characteristic signature of five genes down-regulated in endometriosis when compared to healthy endometrium from women without endometriosis.

Conclusions

The 5-gene expression signature identified in our study had significant predictive power (AUC>0.85) thus suggesting that this marker gene set can be used for a minimally invasive molecular diagnosis of endometriosis. Our data also suggest that the statistical method of five-fold cross validation of differential gene expression analysis procedure can be used for the ability to generate robust gene signatures using real-world clinical data.

Acknowledgments

- Leila Adamyan, MD, PhD, academician of Russian Academy of Sciences, A.I. Evdokimov Moscow State Medical and Dental University, Moscow, Russian Federation
- Assia Stepanian, MD, Academy of Women’s Health and Endoscopic Surgery, Atlanta, Georgia, USA
- Danil Nikitin, MSc, Omicsway Corp., Walnut, CA, USA
- Andrew Garash, MSc, Omicsway Corp., Walnut, CA, USA
- Maria Suntsova, PhD, Omicsway Corp., Walnut, CA, USA
- Maxim Sorokin, MSc, Omicsway Corp., Walnut, CA, USA
- Anton Buadlin, PhD, Omicsway Corp., Walnut, CA, USA

References

EFFECT OF LENGTH OF SURGERY ON THE INCIDENCE OF VENOUS THROMBEMBOLISM AFTER BENIGN HYSSTERECTOMY
Janelle K. Moulder MD MSCR
Wake Forest School of Medicine

Disclosure
● Consultant: Hologic

Objectives
● Identify limitations in current venous thromboembolism (VTE) guidelines
● Use the process to improve VTE thromboprophylaxis with additional risk stratification
● Recognize higher risk patients missed in current protocols

Background
● Venous thromboembolism (VTE) is a leading cause of morbidity and mortality in postoperative patients
● The incidence of VTE following hysterectomy ranges from 0.7—2.2%
● Mechanical and/or pharmacologic prophylaxis is recommended
● Current VTE assessment tools have not been validated in gynecologic surgery patients
● Neither guidelines nor risk assessment tools incorporate newer data that demonstrates additional VTE risk for increasing length of surgery, obesity beyond body mass index of 30, or mode of hysterectomy

Study Objective
● Determine if length of surgery / operative time (OR time) is an independent risk factor for venous thromboembolism (VTE) following benign hysterectomy and determine if differences exist based on age, body mass index (BMI) and surgical approach.

Materials and Methods
● Design: secondary analysis of prospectively-collected surgical quality improvement data
● Setting: American College of Surgeons National Surgical Quality Improvement Database
● Patients or Participants: Patients undergoing abdominal (AH), vaginal (VH), or laparoscopic hysterectomy (LH), identified with Current Procedural Terminology (CPT) codes for benign indications from 1/1/2014—12/31/2017
○ Exclusion Criteria: Patients with cancer, surgery not performed by a gynecologist, not in targeted files, missing OR time, or OR time <30 minutes
Materials and Methods

- Interventions: Patients were compared with respect to incidence of VTE and OR time, stratified by age, BMI, and surgical approach.
- Analyses:
  - Demographics, comorbidities, and surgical characteristics were compared with respect to incidence of VTE, using chi-square, Fisher’s exact test, and Student t tests.
  - Logistic regression was used to estimate the association of OR time and incidence of VTE; OR time was treated as a continuous variable.
  - BMI status, age, and surgical approach were investigated individually.

### Results

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>No VTE</th>
<th>VTE</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>70541 (99.7%)</td>
<td>198 (0.3%)</td>
<td>0.214</td>
</tr>
<tr>
<td>Age in years, mean (SD)</td>
<td>48.1 (10.9)</td>
<td>47.2 (11.0)</td>
<td>0.214</td>
</tr>
<tr>
<td>Race, n (%)</td>
<td></td>
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<tr>
<td>White</td>
<td>46149 (74.4)</td>
<td>122 (7.1)</td>
<td>&lt;0.001</td>
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<td>122 (7.1)</td>
<td>7 (0.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Other</td>
<td>3128 (5.0)</td>
<td>30 (1.6)</td>
<td>0.329</td>
</tr>
<tr>
<td>Missing</td>
<td>8862</td>
<td>88 (4.4)</td>
<td>-</td>
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<td>Hispanic, n (%)</td>
<td></td>
<td></td>
<td></td>
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<td>Yes</td>
<td>109 (62.3)</td>
<td>14 (7.9)</td>
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<td>6221 (9.7)</td>
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<td>BMI, mean (SD)</td>
<td>30.8 (7.6)</td>
<td>32.7 (7.9)</td>
<td>&lt;0.001</td>
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<td>Uterine weight, g, mean (SD)</td>
<td>251.5 (393.7)</td>
<td>283.9 (643.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ASA classification, n (%)</td>
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<td></td>
</tr>
<tr>
<td>1</td>
<td>7271 (10.3)</td>
<td>17 (8.5)</td>
<td>0.028</td>
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<tr>
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<td>47533 (67.1)</td>
<td>124 (62.3)</td>
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<td>3 or 4</td>
<td>16324 (22.6)</td>
<td>93 (46.7)</td>
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<td>Inpatient procedure, n (%)</td>
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<tr>
<td>Yes</td>
<td>33418 (47.2)</td>
<td>134 (67.3)</td>
<td>&lt;0.001</td>
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<tr>
<td>No</td>
<td>37123 (52.8)</td>
<td>64 (32.7)</td>
<td>-</td>
</tr>
</tbody>
</table>

### Conclusions

- Increasing operative time has a cumulative effect on the odds of VTE.
- Odds of VTE are higher for women undergoing an abdominal approach for hysterectomy.
- Odds of VTE are higher for women under age 40.

### Acknowledgments

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### References

CULTURAL AND LINGUISTIC COMPETENCY

Governor Arnold Schwarzenegger signed into law AB 1195 (eff. 7/1/06) requiring local CME providers, such as the AAGL, to assist in enhancing the cultural and linguistic competency of California's physicians (researchers and doctors without patient contact are exempt). This mandate follows the federal Civil Rights Act of 1964, Executive Order 13166 (2000) and the Dymally-Alatorre Bilingual Services Act (1973), all of which recognize, as confirmed by the US Census Bureau, that substantial numbers of patients possess limited English proficiency (LEP).

California Business & Professions Code §2190.1(c)(3) requires a review and explanation of the laws identified above so as to fulfill AAGL's obligations pursuant to California law. Additional guidance is provided by the Institute for Medical Quality at http://www.imq.org

Title VI of the Civil Rights Act of 1964 prohibits recipients of federal financial assistance from discriminating against or otherwise excluding individuals on the basis of race, color, or national origin in any of their activities. In 1974, the US Supreme Court recognized LEP individuals as potential victims of national origin discrimination. In all situations, federal agencies are required to assess the number or proportion of LEP individuals in the eligible service population, the frequency with which they come into contact with the program, the importance of the services, and the resources available to the recipient, including the mix of oral and written language services. Additional details may be found in the Department of Justice Policy Guidance Document: Enforcement of Title VI of the Civil Rights Act of 1964 http://www.usdoj.gov/crt/cor/pubs.htm.

Executive Order 13166, "Improving Access to Services for Persons with Limited English Proficiency", signed by the President on August 11, 2000 http://www.usdoj.gov/crt/cor/13166.htm was the genesis of the Guidance Document mentioned above. The Executive Order requires all federal agencies, including those which provide federal financial assistance, to examine the services they provide, identify any need for services to LEP individuals, and develop and implement a system to provide those services so LEP persons can have meaningful access.

Dymally-Alatorre Bilingual Services Act (California Government Code §7290 et seq.) requires every California state agency which either provides information to, or has contact with, the public to provide bilingual interpreters as well as translated materials explaining those services whenever the local agency serves LEP members of a group whose numbers exceed 5% of the general population.

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If you add staff to assist with LEP patients, confirm their translation skills, not just their language skills. A 2007 Northern California study from Sutter Health confirmed that being bilingual does not guarantee competence as a medical interpreter. http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=2078538.