TABLE 2. Endocrine parameters (mean ± SD)

	Stimulated	Unstimulated	p-value
Follicle stimulation hormone (mIU/mL), day 3	6.33 ± 2.37	5.78 ± 2.08	0.67
Estradiol (pg/mL), day 3	60.43 ± 45.29	35.5 ± 9.25	0.30
Luteinizing hormone (mIU/mL), day 3	5.32 ± 1.81	4.31 ± 2.05	0.35
Anti-Mullerian Hormone (ng/mL)	5.41 ±3.30	3.36 ± 2.43	0.31
Estradiol (pg/mL), day 12	255 ± 103	248.8 ± 26.5	0.91
Progesterone (ng/mL), day 12	0.56 ± 0.29	0.80 ± 0.31	0.18
Luteinizing hormone (mIU/mL), day 12	9.16 ± 6.93	23.48 ± 11.07	0.0031

testing (day 3 FSH, LH, estradiol, and AMH) was measured. Stimulated patients received 2.5 – 7.5mg Letrozole on cycle days 3-7. Unstimulated patients did not receive medication in the follicular phase. Patients were monitored on cycle day 12. Follicular diameter and volume (by Voluson software), endometrial thickness, Doppler blood flow indices (utero-ovarian and perifollicular vessels), serum estradiol, progesterone and LH were measured. Stimulated patients were instructed to take recombinant hCG when dominant follicle reached >16mm and return 36 hours later for IUI. Unstimulated patients underwent IUI 24-36 hours after detecting urinary LH surge. All patients received luteal progesterone.

RESULTS: Both groups had similar age, BMI, and ovarian reserve. The perifollicular pulsatility index (PI) was decreased in the stimulated group compared with unstimulated (1.19 ± 0.72 vs 2.57 ± 2.01, p=0.02, Table 3). The perifollicular resistive index (RI) and S/D ratios showed no difference among the groups. Additionally, ovarian PI, RI, and S/D ratio did not show a difference. Ultrasound measurements of endometrial thickness, follicular diameter, and follicular volume were not different. There were no statistically significant correlations between perifollicular PI and age, BMI, baseline ovarian reserve testing, endometrial thickness, follicular diameter, follicular volume, or periovulatory serum steroid levels.

CONCLUSIONS: Preliminary conclusions from this prospective, ongoing study show that cycles stimulated with aromatase-inhibitor exhibit decreased blood flow impedance as evidenced by a decreased PI compared to unstimulated cycles. Doppler blood flow indices provide a non-invasive means to evaluate ovulation induction cycles. Further research is needed to determine if blood flow indices can predict pregnancy success.

SUPPORT: None.

References:

1. Kurjak et al. *Transvaginal color flow Doppler in the assessment of ovarian and uterine blood flow in infertile women.* Fertil Steril. 1991 Nov;56(5):870-3.
2. Witt MC et al. *Doppler sonography of the uterine and ovarian arteries during a superovulatory program in horses.* Theriogenology 2012 Apr 15;77(7):1406-14.
3. Huey, S et al. *Perifollicular blood flow Doppler indicies, but not follicular pO2, pCO2, or pH, predict oocyte developmental competence in in vitro fertilization.* Fertil Steril 199 Oct; 72(4):707-12.

TABLE 3. Ultrasound parameters (mean ± SD)

	Stimulated	Unstimulated	p-value
Endometrial thickness (mm)	9.3 ± 1.7	10.5 ± 3.0	0.28
Follicular Diameter (mm)	19.8 ± 3.6	19.7 ± 3.2	0.98
Follicular Volume (cm^3)	4.7 ± 3.3	3.6 ± 2.6	0.52
Perifollicular Blood Flow Indices			
S/D Ratio	5.17 ± 7.86	3.04 ± 3.08	0.61
Pulsatility Index	1.19 ± 0.72	2.57 ± 2.01	0.024
Resistive Index	0.75 ± 0.47	0.75 ± 0.22	0.99
Utero-ovarian Blood Flow Indices			
S/D Ratio	15.45 ± 23.42	4.03 ± 1.81	0.35
Pulsatility Index	4.75 ± 8.15	1.72 ± 0.74	0.47
Resistive Index	1.10 ± 0.90	0.71 ± 0.12	0.41

P-72

HIGH PREVALENCE OF ENDOMETRIOSIS IN PATIENTS WITH HISTOLOGICALLY PROVEN ADENOMYOSIS. M. Facadio Antero,[a] D. O'Sullivan,[b] S. Mandavilli,[c] J. Mullins.[b] [a]Department of Obstetrics/Gynecology University of Connecticut School of Medicine, Farmington CT, USA; [b]Department of Obstetrics/Gynecology Hartford Hospital, Hartford, CT, USA; [c]Pathology Department Hartford Hospital, Hartford, CT, USA.

BACKGROUND: Adenomyosis and endometriosis are conditions defined by growth of endometrial glands in the myometrium and in extra uterine tissue respectively. Both diseases cause dysmenorrhea and pelvic pain. Previous studies suggest a significant association between adenomyosis and peritoneal and deep infiltrating endometriosis in infertile women.[1,2] However, the prevalence of a dual diagnosis is difficult to determine secondary to the difficulty in establishing a diagnosis of adenomyosis and in differentiating between the two diseases clinically. Knowing the prevalence and risk factors for dual diagnosis is important for counseling patients on treatment options, since hysterectomy may not be curative, as well as the implications it has on future fertility.

OBJECTIVE: To determine the prevalence of endometriosis in histologically-proven adenomyosis patients with either dysmenorrhea or pelvic pain and identify potential risk factors for having both adenomyosis and endometriosis.

MATERIALS AND METHODS: This was a single institution cross-sectional study including data from 2008-2016. Patients with either dysmenorrhea or pelvic pain and histologically-proven adenomyosis at the time of hysterectomy were identified by reviewing operative and pathology reports. The diagnosis of endometriosis was determined and data regarding demographic and risk factors was obtained by reviewing the medical record, pathology reports, and intraoperative findings. Patients with cancer or hyperplasia in their final pathology were excluded. Chi squared, t-test, and univariate logistic regression were used to analyze the data.

RESULTS: A total of 300 patients were included. Endometriosis was present in 127/300 (42.3%). Among these, 67/127 (52.7%) had no known history of endometriosis. Dual diagnosis patients were more likely to be Caucasian (79% vs 58.5%, p<0.001), have adhesions at the time of surgery (OR 3.28, 95% CI 2.029-5.304), and have both dysmenorrhea and pelvic pain (OR 2.163, 95% CI 1.317-3.551). These patients were less likely to have menorrhagia (OR 0.54 95% CI 0.336-0.868), fibroids (OR 0.540 95% CI 0.340-0.0.859) and bilateral tubal ligation (OR 0.616 95% CI 0.381-0.993).

CONCLUSION: There is a high prevalence of endometriosis in patients with adenomyosis who present with either dysmenorrhea or pelvic pain. Risk factors for dual diagnosis include presence of both symptoms, adhesions, and Caucasian race. Results show that it is often difficult to make the diagnosis of endometriosis in setting of adenomyosis given the high percentage of undiagnosed endometriosis in this patient population.

SUPPORT: No financial support was used for the completion of this study.

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1. Kunz G, Beil D, Huppert P and Leyendecker G, Structural abnormalities of the uterine wall in women with endometriosis and infertility visualized by vaginal sonography and magnetic resonance imaging. Hum Reprod 15, 76–82.
2. Di Donato N, Montanari G, Benfenati A, Leonardi D, Bertoldo V, Monti G, Raimondo D, Seracchioli, Prevalence of adenomyosis in women undergoing surgery for endometriosis. R.Eur J Obstet Gynecol Reprod Biol. 2014 Oct;181:289-93.

P-73

LARGE-SCALE HETEROGENEOUS DISRUPTION OF SPERM DNA-METHYLATION IN INFERTILE INDIVIDUALS IS ASSOCIATED WITH GENES IMPLICATED IN SPERM CHEMOTAXIS, ACROSOME REACTION AND EGG-BINDING. Philip J. Uren,[a] La-Toya Williamson,[a] Mike Karsian,[a] Douglas Carrell,[b] Andrew D. Smith,[c] Alan Horsager.[a] [a]Episona, Inc., Pasadena, CA, USA; [b]University of Utah, Salt Lake City, UT, USA; [c]University of Southern California, Los Angeles, CA, USA.

BACKGROUND: The standard of care for assessing male fertility is the semen analysis. In addition to checking for low sperm counts, gross morphological disruptions or a lack of progressive motility can be examined for. However, many infertile men have normal semen parameters. In these cases, sperm function may be impacted in less visually obvious ways.

OBJECTIVE: To identify and characterize patterns of aberrant DNA methylation in sperm samples from infertile males suspected of impacting genes associated with sperm functions other than morphology and motility.

MATERIALS AND METHODS: We defined a reference sperm methylomes from 156 samples derived from 98 unique donors of known fertility. We compared the DNA methylation profiles of 336 sperm samples from 292 unique infertile men to identify loci with substantial variation from the reference. Sperm DNA methylation was measured using Illumina's 450k HM array. We called a gene differentially methylated in an infertile sample if two or more probes in the gene body or 5kb upstream of the transcription start site showed a methylation level that was 0.2 higher/lower than 95% of the fertile control samples, and showed statistically significant association with fertility potential under hold-one-out cross-validation. The analyzed samples were a combination of those used in Aston et. al (2015), and 264 new samples collected from Episona's partner sperm banks (known-fertile samples) and fertility clinics (infertile samples). Infertile samples were collected from couples with no known female-factor impacting their infertility and normal semen analysis parameters.

RESULTS: 37% of infertile samples examined had one or more genes differentially methylated by the above criteria. Most samples with differential methylation had only 1 or 2 differentially methylated genes (145 samples), while a minority had very large counts (16 samples had more than 100 differentially methylated genes). Common differentially methylated genes included FCGBP (differentially methylated in 22 samples; putatively involved in sperm–zona pellucida interaction), ID3 (20 samples; known role in murine male infertility) and a region containing two taste receptors-TAS2R60 and TAS2R41 (28 samples; speculated to be involved in sperm chemotaxis). In other cases, such as the gene TBCD (37 cases), the role in fertility is less clear.

CONCLUSIONS: Our data support the hypothesis that male-factor infertility is multi-faceted, with many different potential underlying causes. We have taken initial steps to identify common epigenetic disruptions that are likely to be associated with male-factor infertility, but which don't impact morphology or motility and hence may be difficult or impossible to identify by standard semen analysis methods.

FINANCIAL SUPPORT: PJU, LW, MK and AH are employees of Episona, Inc.; MA is an intern at Episona, Inc.

Reference:

1. Aberrant sperm DNA methylation predicts male fertility status and embryo quality KI Aston, PJ Uren, TG Jenkins, A Horsager, BR Cairns, AD Smith, DT Carrell Fertility and Sterility, Volume 104, Issue 6, 1388 - 1397.e5

P-74

ABNORMAL CLEAVAGE PATTERNS IN EMBRYOS ARE ASSOCIATED WITH ANEUPLOIDY AND POOR MORPHOLOGY SCORES. Jacqueline Ho,[a] Wael Salem,[a] Nabil Arrach,[b] Kristin Bendikson,[a] Karine Chung,[a] Richard Paulson,[a] Ali Ahmady.[a] [a]Department of Obstetrics & Gynecology, USC Keck School of Medicine, Los Angeles, CA; [b]Progenesis Inc., La Jolla, CA.

BACKGROUND: Morphokinetic parameters as measured through time-lapse imaging may predict embryonic developmental potential. While there are several studies on the timing of early cell divisions, there are limited data on abnormal cleavage (AC) events and their relationship to embryo quality. An AC is the division from a mother blastomere cell to three daughter cells. This is thought to be secondary to abnormal mitotic spindle assembly, leading to an abnormal segregation of chromosomes. Previous studies report that embryos exhibiting ACs have decreased blastulation and worse implantation rates. In our study, we sought to determine if ACs are associated with aneuploidy. We also evaluated the relationship between ACs and developmental potential as well as day 3 and day 5 morphologic scoring.

OBJECTIVES: Our primary objective was to determine if ACs are related to ploidy status. Secondary objectives were to determine if ACs are correlated with blastulation rates and with embryo morphologic scores at the cleavage and blastocyst stages.

MATERIALS AND METHODS: Previously cryopreserved human embryos donated for research were thawed and cultured in the Miri Time-lapse incubator for 6 days. A staff embryologist recorded standard time-lapse parameters and day 3 and 5 morphology assessments. Trophectoderm biopsies were performed on embryos that grew to blastocysts on day 5 or 6. Otherwise whole embryos were sent for preimplantation genetic screening (PGS). Next generation sequencing was used to determine embryo ploidy status. Morphologic grading of embryos was performed per Society of Assisted Reproductive Technology guidelines for cleavage stage embryos. We used methods for blastocyst morphologic grading described by Gardner, et al with minor modifications. Statistics were performed using Chi-square, Fisher's Exact, ANOVA, and logistic regression.

TABLE 1. Bivariate Analysis of Abnormal Cleavage Events, Blastocyst Development, and Morphologic Score on Euploid vs. Aneuploid Status

	Odds Ratio (95% CI)[b]	P-value[a]
Any Abnormal Cleavage (AC)	0.04 (0.01-0.22)	<0.001[a]
AC – 1st	0.06 (0.01-0.37)	0.003[a]
AC – 2nd	0.02 (0.002-0.22)	0.001[a]
Multiple ACs	0.08 (0.01-0.86)	0.04[a]
Blastocyst formed	9.0 (2.1-37.9)	0.003[a]
Day 3 Morphology (Poor vs. fair/good)	0.94 (0.2-4.4)	0.93
Day 5 Morphology (Poor vs. fair/good)	0.0 (0-0.46)	0.02[c]

a. Logistic regression used, $p<0.05$ considered significant
b. Odds ratios with 95% confidence interval reported
c. Fisher's Exact Test used, $p<0.05$ considered significant

RESULTS: 50 embryos were included our analysis. 32/50 (64%) of thawed embryos grew to the blastocyst stage. 35/50 (70%) of embryos were euploid. ACs were visualized in 15/50 (30%) embryos. 8/15 (53.3%) of these embryos experienced an AC after the 1st cytokinesis. 7/15 (46.7%) of embryos had ACs after the 2nd cytokinesis. 4/15 (26.7%) embryos had more than 1 AC event. Aneuploid embryos had a significantly higher percentage of AC events (73.3% vs 22.9%, $p<0.001$). AC events did not reliably predict which embryos grew to the blastocyst stage or those that arrested. Embryos that had at least 1 AC took an average of 10.7 hours longer to develop from a morula to a fully expanded blastocyst compared to those without ACs ($\beta=10.7$, $p=0.01$). Cleavage stage morphology scores did not correlate with ACs. In blastocysts with ACs, there was a higher proportion of poor quality embryos compared with good/fair embryos (66.7% vs 33.3%, $p=0.03$).

CONCLUSIONS: Based on our findings, ACs were more likely to occur in aneuploid embryos. While they did not predict blastocyst formation, they were associated with delayed blastulation and with poor blastocyst morphology scores. When selecting embryos for transfer, particularly those not undergoing PGS, those with ACs may have a worse prognosis for achieving a successful pregnancy.

FINANCIAL SUPPORT: Prognosis, Inc. (La Jolla, CA).

P-75

IMPACT OF PATIENT PREFERENCE ON RATE OF DOUBLE EMBRYO TRANSFER AND RESULTANT TWIN GESTATION. C. C. Shenoy, A. Ainsworth, T. Jones, M. Purdy, D. Morbeck, J. Jensen, C. C. Coddington. Department of Obstetrics and Gynecology, Mayo Clinic, Rochester, MN.

BACKGROUND: Significant strides have been made in the United States to encourage single embryo transfer and minimize the occurrence and resultant risks associated with twin gestations. While the medical community has recognized the need for refinement and demonstrated the success of single embryo transfer, patient choice and education remains a significant factor in reproductive medicine and resultant obstetrical outcomes.

OBJECTIVE: This study aims to assess the impact of patient choice on number of embryo transfer and resultant twin gestation.

MATERIALS AND METHODS: Patients undergoing in vitro fertilization (IVF) between 2013 and 2016 at Mayo Clinic, Rochester were reviewed. Patients under 35 who received a double embryo transfer, which resulted in a twin pregnancy, were included in this review. The embryo transfer consent forms and transfer reports were reviewed. The planned number of embryos transferred, actual number of embryos transferred and embryo grade were assessed. Consent forms for number of embryos to transfer are signed prior to starting an IVF cycle. Our practice is to encourage good prognosis patients to consent to transfer 1-2 embryos, allowing the final decision on whether to transfer one or two embryos to be made by the embryology and physician team after assessment of embryo quality on day of transfer. If grade A blastocysts are in culture, a single embryo is transferred. Subsequent clinical pregnancy rate, including number of fetal heart beats, was calculated.