



Ian Donald International University School of Medical Ultrasound

In cooperation with



World Association of Perinatal Medicine



Dubrovnik Libertas International University

**3<sup>rd</sup> GLOBAL CONGRESS  
OF IAN DONALD SCHOOLS**  
– World Congress –



**19<sup>th</sup> – 21<sup>st</sup> June 2015**  
**T-Hotel, Cagliari, Sardinia, Italy**

*In memory and honour of Maria Angelica Zoppi*

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# ABSTRACTS

**The 3 winners of the 1,500 Euros prizes are:**

**Natural History of Cesarean Scar Pregnancy: Can We Predict Outcome?**

*Minneci G, Timor-Tritsch IE, D'Antonio F, Foti F, Izzo T, Forlani F, Cali G*

**Amniocentesis in Dichorionic Twin Pregnancies does not Increase the Risk of Adverse Outcome Until 24 weeks**

*Caramellino L, Viora E, Pertusio A, Sciarrone A, Volpi E, Gaglioti P, Todros T*

**Double Stimulation in a Single Menstrual Cycle Increases the Number of Oocytes Collected in Poor Prognosis Patients undergoing IVF Treatment. Prospective Study with Historical Control**

*Vaiarelli A, Rienzi L, Colamaria S, Alviggi C, Trabucco E, Zullo F, Giuliani M, Gravotta E, Sapienza F, Cimadomo D, Capalbo A, Ubaldi FM*

## Natural History of Cesarean Scar Pregnancy: Can We Predict Outcome?

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### OBJECTIVE

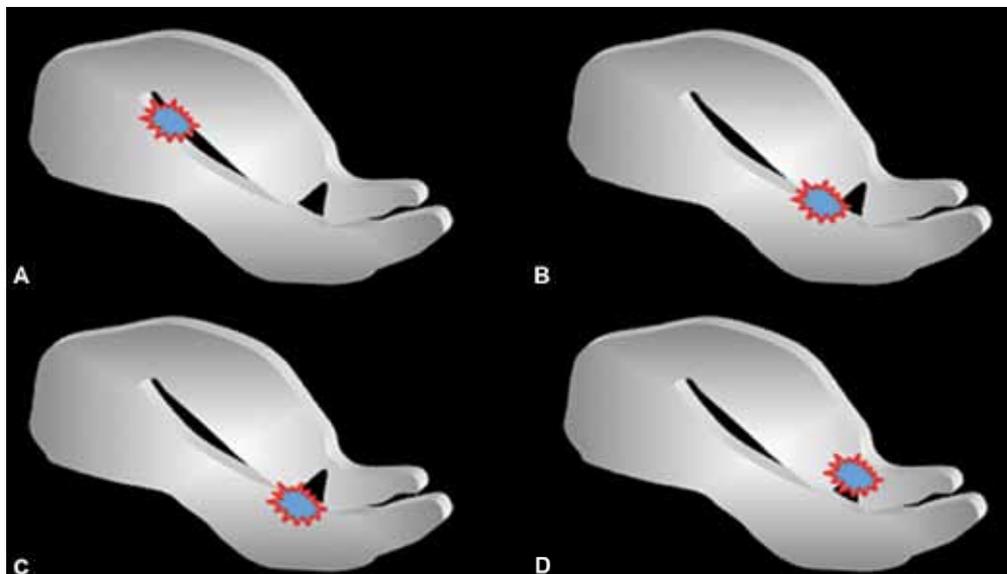
To prospectively predict and counsel patients about their diagnosed cesarean scar pregnancies (CSP) based upon a 5.0 to 7.6 weeks transvaginal ultrasound examination. We suggest that it is possible to distinguish between the CSP which could evolve to fetal viability with morbidly adherent placenta (MAP) and the ones leading to miscarriage or uterine rupture.<sup>1,2</sup> The aim of our study is to identify ultrasonographic criteria for differentiation of these conditions.

### METHODS

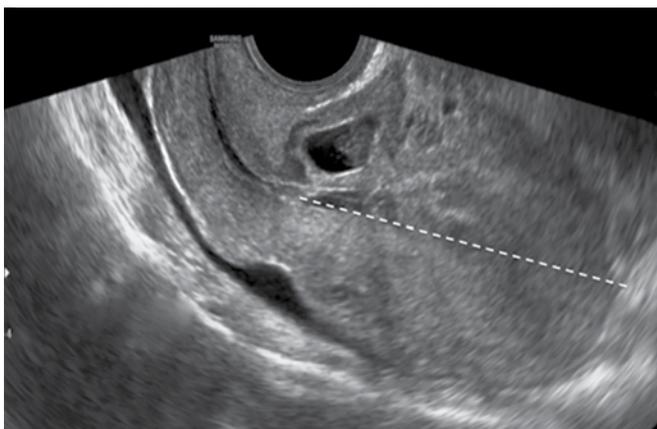
This is a retrospective study including 75 cases of MAP observed between January 2004 and April 2015. Their ultrasound scans performed at 5.0 to 7.6 weeks of gestation were reviewed. Thirty-five of them evidenced the spatial relation between gestational sac and scar/niche. We defined the implantation as:

- 'away from' the scar: intrauterine pregnancy with normal implantation;
- 'in' the scar: the gestational sac is inside the niche, which frequently is not visible;
- 'on' or 'next to' the scar: the gestational sac is in contact with or close to the scar (Figs 1A to D).<sup>3</sup>

An imaginary line was drawn longitudinally crossing the uterine cavity from the internal uterine orifice to the fundus and the location of the sac was determined upon the above criteria (Figs 2 and 3).



**Figs 1A to D:** (A) Away from the scar, (B) next to the scar, (C) on the scar and (D) in the scar/niche



**Fig. 2**



**Fig. 3**

## RESULTS

Ultrasound pictures of 35 patients were found eligible for the study. In all these cases, the gestational sac was situated 'on' or 'next to' the scar. None of them revealed that the position of the sac was 'away from' or 'in' the scar. In all cases, more than 1/3 of gestational sac was behind the line we drawn.

## CONCLUSION

Our study provides useful information to predict that in case of implantation 'on' or 'next to' the scar, the pregnancy can evolve to the third trimester with MAP and fetal viability, while in cases where the localization of the sac is 'in' the scar the risk of miscarriage and uterine rupture is elevated.

We suggest in all pregnant women with previous cesarean surgery, an ultrasound scan at 5.0 to 7.6 weeks in order to:

- early diagnose CSP
- differentiate the sac localization 'in', 'on' or 'next to' the scar for an optimal counseling to patients.

Prospective multicenter studies with bigger data collection could confirm our hypothesis.

## REFERENCES

1. Timor-Tritsch IE, et al. Cesarean scar pregnancy is a precursor of morbidly adherent placenta. *Ultrasound Obstet Gynecol* 2014
2. Timor-Tritsch IE, et al. Cesarean scar pregnancy and early placenta accreta share common histology. *Ultrasound Obstet Gynecol* 2014
3. Naji O, et al. Does the presence of a cesarean section scar affect implantation site and early pregnancy outcome in women attending an early pregnancy assessment unit? *Human Reprod* 2013;0(0):1-8.

# Amniocentesis in Dichorionic Twin Pregnancies does not Increase the Risk of Adverse Outcome Until 24 Weeks

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## INTRODUCTION

The literature about abortion risk following amniocentesis in twin pregnancies is not univocal: some authors identify a risk almost double in twin *vs* single pregnancies, while others argue that post-amniocentesis fetal loss rate is similar in twin and single pregnancies (about 1%).

The aim of our study is to compare the risk of fetal loss and PROM < 24 weeks between twin dichorionic pregnancies undergoing amniocentesis and a control group including twin dichorionic pregnancies undergoing sonography only at the same gestational age.

## MATERIALS AND METHODS

We analyzed 327 dichorionic twin pregnancies referred to Sant'Anna Hospital, Turin, Italy.

Among them we identified a study group of 163 twin pregnancies who performed amniocentesis by experienced operators and a control group of 164 women with twin pregnancies who performed only ultrasound scan at the same gestational age (16 ± 1.38 weeks).

Triplets, selective feticide, abnormal fetal karyotype and fetal malformations were not included in the study.

All data concerning amniocentesis was collected by our ultrasound database (Echoplus), and the follow-up was carried out by using the computerized database.

## RESULTS

The mean age was 36.82 ± 3.9 (19–46) years for cases and 36.10 ± 5.1 (20–46) years for controls, with no statistically significant difference between the two groups.

The mean gestational age at the time of amniocentesis was 16.6 ± 1.38 (15–22) weeks.

Indications for amniocentesis were: 75.5% maternal age; 12.8% abnormal first trimester screening; 4.9% growth restriction of one or both fetuses; 3.5% suspicion of mosaicism at CVS; 3.3% fetal malformation.

In both groups, we observed an overall risk of fetal loss and PROM of 1.8%: in the study group, we observed one case of spontaneous abortion before 20 weeks, one of spontaneous abortion between 20 and 24 weeks and one PROM before 20 weeks of gestational age.

In the control group, we observed three cases of PROM before 20 weeks of gestational age.

There was not a significantly increased risk of these complications in women who performed amniocentesis.

## CONCLUSION

Despite the sample size and the retrospective nature of our study, we found no difference in PROM and spontaneous abortion in dichorionic twin pregnancies exposed to genetic amniocentesis compared with a similar population of dichorionic twin pregnancies who underwent sonographic scans only.

Our data agree with a recent prospective observational study (Lenis-Cordoba, 2013) on fetal loss risk following amniocentesis in twin dichorionic pregnancies: these favorable results can be helpful for the clinician who faces counseling to the couples about amniocentesis.

## Double Stimulation in a Single Menstrual Cycle Increases the Number of Oocytes Collected in Poor Prognosis Patients undergoing IVF Treatment: Prospective Study with Historical Control

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## OBJECTIVE

The antral follicle development in human ovary seems to be characterized by 2 to 3 waves during an interovulatory interim, as reported in animal species. This evidence overtakes the common theory that a single cohort of antral follicles grows only during the follicular phase of a menstrual cycle. According to this observation, a new model for controlled ovarian stimulation (COS) and oocyte retrieval strategy has been proposed: a double COS during a single menstrual cycle (DUOSTIM). The rationale of this approach is to increase the number of oocytes and embryos available per menstrual cycle in poor prognosis patients.

## DESIGN

The aim of this prospective study with historical control is to compare the standard stimulation approach *vs* the DUOSTIM. Seventeen patients with sub-optimal response in previous in vitro fertilization (IVF) treatment after standard stimulation protocol were enrolled to undergo a DUOSTIM with antagonist protocol and starting maximal doses of gonadotropins. The primary outcome is the number of cumulus-oocyte complexes (COCs) retrieved and mature oocytes (MII oocytes). The secondary outcome is the number of blastocysts obtained.

## MATERIALS AND METHODS

The time span between the standard stimulation cycle (control group, n = 17) and the DUOSTIM (study group, n = 17) was ≤ 6 months. The inclusion criteria were: less than 7 COCs retrieved in the previous IVF cycle, AMH ≤ 1.6 ng/ml and AFC ≤ 7. After the first oocyte retrieval, the second COS was started a 5 days later. All oocytes retrieved were microinjected with a single spermatozoa and all embryos obtained were frozen at the blastocyst stage. Paired t-test and McNemar's test were used to compare continuous and categorical variables, respectively. Alfa was set at 0.05.

## RESULTS

	Control group	Stim 1	Stim 2	DUOSTIM (stim1 + 2)
Age	37.71 ± 3.22	38.24 ± 3.35		
AFC	4.38 ± 2.16	4.23 ± 2.17		
AMH	0.63 ± 0.47	0.59 ± 0.39		
COCs	4.06 ± 1.55	4.72 ± 1.78	5.0 ± 2.70.	9.72 ± 3.39*
MI	3.22 ± 1.48	2.89 ± 1.81	3.5 ± 1.79	6.11 ± 3.03*
Blastocysts	0.78 ± 0.73	0.94 ± 1.16	1.16 ± 1.33	2.56 ± 2.15*

\*p < 0.01 for comparisons with control group; All other comparisons are not significantly different

## CONCLUSION

The knowledge of multiple follicle waves within a menstrual cycles may open new approaches in treating patients with reduced ovarian reserve. The number of oocytes retrieved, in fact, together with the age of the patient is one of the most important factor to predict the live birth of a healthy baby. The possibility to increase the number of retrieved oocyte per menstrual cycle could increase the chance for a pregnancy per menstrual cycle, improving the efficacy of the IVF procedure. According to our preliminary results, we significantly increased the number of MII oocytes retrieved and of the blastocysts obtained in the study group suggesting the DUOSTIM an alternative option to increase the efficacy of an IVF procedure.



## Rare Causes of Acute Abdomen in Pregnancy; 'Ultrasound to the Rescue': A Review of Two Cases

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### ABSTRACT

Acute abdomen in pregnancy poses special challenge to the pregnant woman, her unborn infant and the attending physician. The problems are multifactorial as the physiological changes in pregnancy mask some of the clinical signs that can be elicited to help in making accurate diagnosis. Some diagnostic modalities are not feasible in pregnancy because of the presence of the fetus. Another dilemma is that two lives are at stake. It becomes even more challenging when one is faced with rare causes. It is for these reasons that the choice of diagnostic modality becomes critical. The chosen diagnostic modality should be readily available, noninvasive, least hazardous to the mother and fetus but at the same time provide adequate information to enable accurate diagnosis. Ultrasonography provides such an opportunity and should be utilized wherever the need arise.

We present two cases of acute abdomen in pregnancy managed at Abubakar Tafawa Balewa University Teaching Hospital.

### CASE REPORTS

#### Case 1

Mrs SA was a 28 years old G6P4 +0, with 3 living children. She presented at 33 weeks + 6 days with severe left lumbar region pain and constipation, a viable fetus at 35 weeks lying transverse and a large cystic tender mass and absent bowel sounds (Figs 1 to 3).

An urgent (2D) ultrasound was done and the findings were: a viable fetus lying transverse at 35 weeks gestation and reduced liquor volume and a huge hydronephrotic left kidney (Figs 4 and 5).

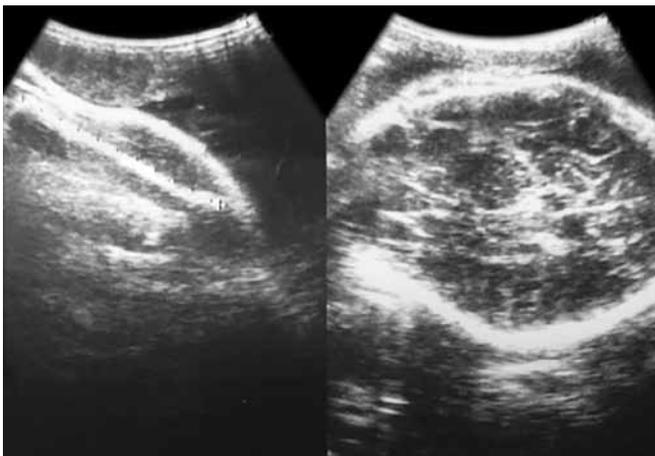


Fig. 1: EGA assessment with FL and BPD

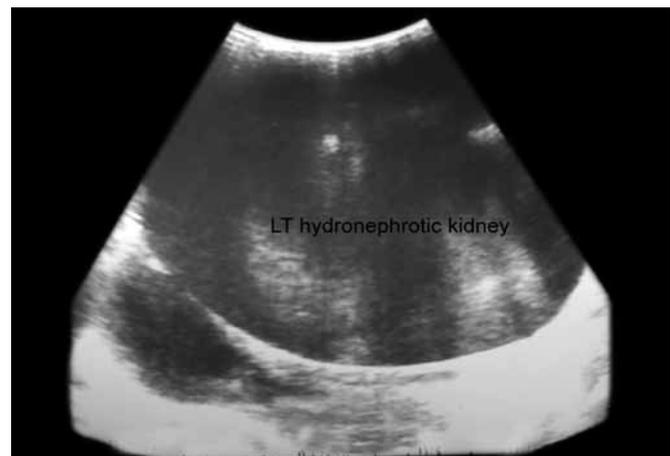


Fig. 2: Huge hydronephrotic left kidney

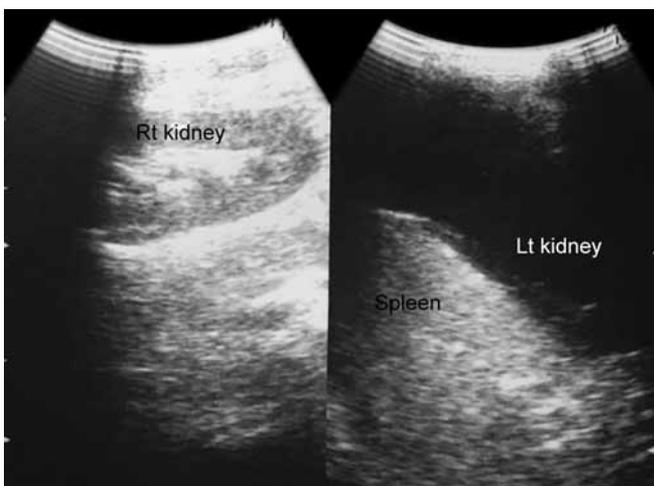


Fig. 3: Normal right kidney and hydronephrotic left kidney

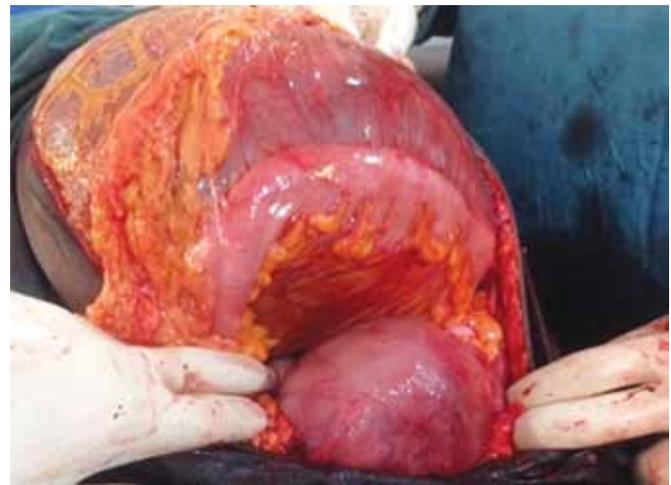
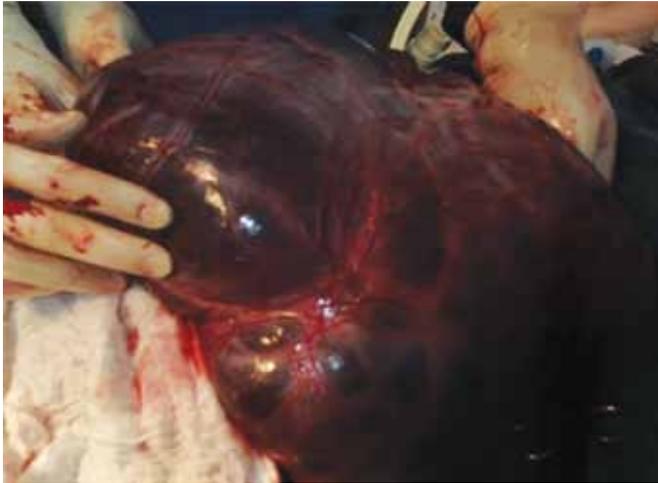


Fig. 4: The gross picture of the left cystic kidney attached to the omentum and the transverse colon and a protruding gravid uterus

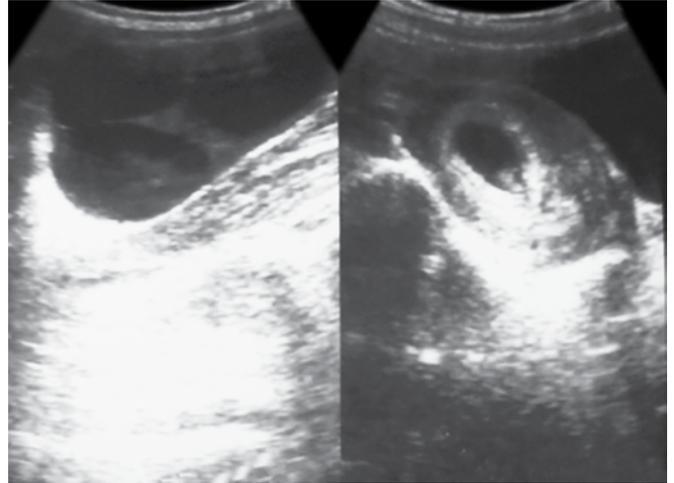
**Case 2**

Mrs MZ a 21 years old primigravida presented with severe right sided lower abdominal pain and fainting attacks at 7 weeks, 4 days pregnancy and cystic and tender right iliac fossa mass.

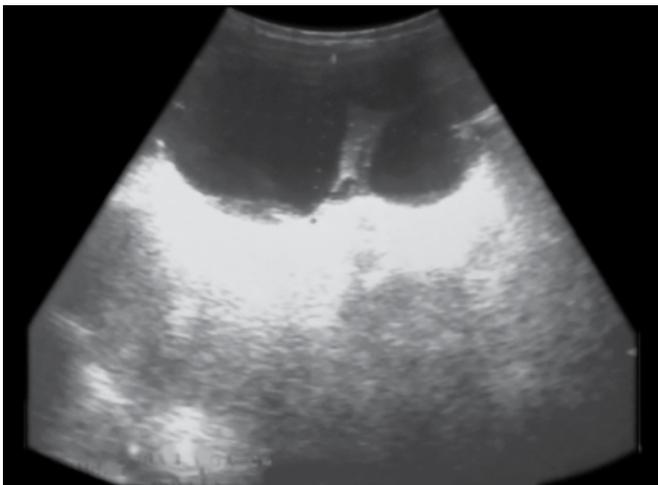
An urgent 2D scan revealed an intact gestational sac with fetal echo (Fig. 6), at 7 weeks + 2 days, a right multiseptate ovary 10 × 9.2 cm (Fig. 7).



**Fig. 5:** The affected kidney with multiple cysts after removal



**Fig. 6:** A multiseptate cystic ovary (left) and a gravid uterus with fetal echo (right)



**Fig. 7:** A multiseptate ovary



**Fig. 8:** The gross picture of the affected and the gravid uterus



**Fig. 9:** Grossly normal looking tubes bilaterally and a grossly normal looking ovary on the right side of the picture



**Fig. 10:** Gross specimen of the cyst after cystectomy

The review is meant to alert obstetricians on the critical role of ultrasound in enhancing accurate diagnosis in the face of a complex clinical condition like acute abdomen in pregnancy (Figs 8 to 10).

## CONCLUSION

Ultrasound is an effective tool in making accurate diagnosis of the course of acute abdomen in pregnancy in experienced hands. It is safe, relatively inexpensive, and versatile technique that is readily available.

## Ultrasonic Evaluation of Fetal and Newborn Gynecologic Disorders

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Ultrasound examination of children's pelvis is completely different from that of adults: (1) the probe to be used has to be adjusted to the age and habitus of the child and the organ to be ensonated. (2) The requirement for a full bladder can be replaced by putting water in the vagina, rectum, cloaca or utricule or last option instilling water into the urinary bladder through a catheter. (3) The uncooperative child may be distracted by a toy or by sucking on mother's breast while she cuddles child as ultrasound examination is going on. Giving sedatives or anesthesia is seldom done unless the child has a disorder and cannot keep still. (4) The absence of identifiable reference landmarks can be remedied by use of Doppler ultrasound to identify the blood vessel next to the organ in question. Transabdominal ultrasound may not give the best resolution, so a transrectal ultrasound can be done using the vaginal probe. The technique of transperineal sonography is described; illustrated by a few cases. Different cases are shown, such as congenital anomalies of the generative tract, such as ureterocele, imperforate hymen, transverse vaginal septum, cloacal malformation, double uterus (OHVIRA), ambiguous genitalia, clitoromegaly and confirmation of the presence of uterus and ovaries. Tumors of the ovary either benign or malignant are shown with ultrasound images, gross pathology on excision and finally histopathologic examination. Fetal ovarian cyst diagnosed *in utero* and managed at birth. Breast ultrasound of the preterm neonate, full term neonate, stage I to V Tanner stages, correlated with the ultrasound of the uterus, cervix and ovaries.

## Pseudoaneurysm of Uterine Artery: Report of a Case

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<sup>8</sup>G Cossu, <sup>9</sup>A Vannini, <sup>10</sup>G Nieddu, <sup>11</sup>G Ruiu, <sup>12</sup>M Vallone

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## INTRODUCTION

The pseudoaneurysm of uterine artery is the result of an incomplete laceration of the arterial wall with consequent blood transition to the perivascular tissue that, thanks to blood pressure, produces a pocket-communication with the vascular lumen.

## CASE REPORT

A 33 years old female, p 0000, was controlled at 34 weeks of gestation because of uterine contractions.

The cervix ultrasonography examination showed, in the rear lip, an anechoic mass with intensely positive color Doppler and high-speed swirling flow.

The 36 weeks control showed an anechoic mass to the cervical myometrium in which was detectable a pulsating mass with like arterial flow.

At 37 weeks of gestation, the patient was subjected to cesarean section in which occurred a severe metrorrhagia, with cervix origin, that was stopped by using hemostatic balloon.

After 2 days, the balloon was deflated with consequent metrorrhagia that was stopped by inflating the balloon.

The patient was subjected to embolization of the cervical branch of uterine artery by contralateral access. This process stopped bleeding even after balloon removal and it caused a progressive reduction of the volume swelling almost to its disappearance at 6 months.

The patient had not amenorrhea or symptoms linked to the embolization process.

## DISCUSSION

The pseudoaneurysm of uterine artery should be included in the differential diagnosis of postpartum hemorrhage specially after cesarean section and even after hysterectomy.

The transvaginal ultrasonography examination and the color Doppler are indispensable both in the diagnosis and in the management of this virtually lethal pathology.

Hysterectomy was the classic treatment but nowadays the uterine artery embolization is considered the first therapeutic option because of its efficiency and safety.

## Fetal Supraventricular Tachycardia with and without Non-Immune Fetal Hydrops: Two Cases Diagnosis and Management

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### INTRODUCTION

Abnormal fetal heart rate (FHR) patterns are detected in 0.2 to 2% of pregnancies and significant arrhythmias are present in the 10% of these cases. The vast majority being intermittent extrasystoles which have little clinical relevance. Less than 10% of referrals are due to sustained tachy- or bradyarrhythmias and they are clinically important. Supraventricular tachycardia (SVT) and atrial flutter (AF) are most frequent causes of fetal tachycardia. Fetal heart rates in SVT most commonly range from 200 to 300 bpm, is either paroxysmal or incessant in nature. In 36 to 64% is associated with nonimmune fetal hydrops (NIHF) with a high incidence of perinatal mortality. The choice of therapy depended on the fetal condition, arrhythmia characteristics, gestational age, maternal health, and willingness to undergo treatment. Prenatal treatment is not randomized and although if antiarrhythmic therapy (Digoxin, Fleicanide, Sotalol) administered to the mother with transplacental passage to the fetus, is effective in most cases, sometimes the management of these cardiac rhythm disturbances was difficult because of association to NIHF and circulatory compromise that need prompt intervention. We want to report two cases of SVT before 35 weeks of gestation with and without NIHF and their management.

### MATERIALS AND METHODS

Case I: Secondgravida primipara, 36 years old, with fetal SVT diagnosed at 33 weeks with NIHF (hydrothorax and ascites). Fetal echocardiogram: FHR 272 bpm. An immediate cesarean section was performed: 2000 gm girl with Apgar scores 6 at 1 minute and intubated at 5 minute.

Case II: Primigravida, 38 years old, fetal SVT without NIHF diagnosed at 26 weeks. Fetal echocardiogram: FHR 232 bpm. The patient was started on fleicanide and digoxin therapy. Fetal echocardiogram at 35 weeks: sinus rhythm. Hospitalized at 38 weeks for premature rupture of membranes. Drug therapy was stopped before delivery. She had a cesarean section on cardiologic indication as a live male, 3080 g Apgar score 9 to 10, at 1 and 5 minute.

### RESULTS

Case I: Despite intensive cardiopulmonary resuscitation, the infant died at 8 days after 2 recidives.

Case II: Postnatal echocardiogram was normal and the electrocardiogram showed sinus rhythm. Regular neurologic development at 1 year of follow-up.

### CONCLUSION

Fetal SVT, especially if associated to NIHF, has a high fetal mortality. Currently, there are not standard guidelines for fetal SVT management. Specific strategy and multicentric studies are needed which would focus on the definitive treatment of fetal SVT and taken a close collaboration between obstetricians and pediatric cardiologists into consideration on follow-up mother and fetus.

## Sonographic Assessment of Fetal Profile Anomalies: Report of 53 Cases

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### INTRODUCTION

Prenatal recognition of facial anomalies during pregnancy can lead to the diagnosis of various genetic syndromes and chromosomal anomalies. Among these malformations, ultrasound examination allows the recognition of fetal microretrognathia, flat profile and cleft lip/palate.

Aim of our study was to evaluate if measurement of facial angles improves the sensitivity of ultrasound to identify normal or abnormal fetal profile and, in presence of craniofacial anomalies, to diagnose microretrognathia, flat profile and cleft lip/palate.

### MATERIALS AND METHODS

In this prospective study, we recruited 53 fetuses with ultrasound diagnosis of craniofacial anomalies (19 cases of microretrognathia, 21 cases of flat profile and 13 cases of cleft lip/palate) confirmed at birth or at autopsy, and 53 normal fetuses at 19 to 26 weeks' gestation.



The mid-sagittal fetal cranial view was obtained by 2D scan and then a 3D volume was acquired. Multiplanar reconstruction allows to measure two angles:

- The inferior facial (IF) angle, defined by the crossing of the line orthogonal to the vertical part of the forehead at the level of the synostosis of the nasal bones and the line joining the tip of the mentum and the anterior border of the more protruding lip;
- The maxilla-nasion-mandible (MNM) angle, defined as the angle between the intersection of the maxilla-nasion and mandible-nasion lines.

Subjective evaluation of fetal profile by a senior sonographer was compared, double blinded, with the measurement of IF and MNM angles.

## RESULTS

The detection rate for the craniofacial anomalies (micro-retrognathia, flat profile and cleft lip/palate) was 88.6% with subjective evaluation performed by a senior sonographer, 50.9% with IF angle and 64.1% with MNM angle.

As for microretrognathia, the detection rate was 73.6% with subjective evaluation of senior sonographer, 53.3% with IF angle and 60% with MNM angle.

The detection rate of flat profile was 92% with senior sonographer evaluation, 47.6% with IF angle and 47.6% with MNM angle.

Lastly, for cleft lip/palate, the detection rate was 92.3% with subjective evaluation, 38.4% with IF angle and 92.3% with MNM angle.

## CONCLUSION

In our experience, the detection rate of fetal facial anomalies is higher with a subjective examination performed by a senior sonographer than with the measurement of IF and MNM angles. In presence of cleft lip/palate, MNM angle has the same accuracy of subjective evaluation.

## Counseling for Female HPV-Infection of Child Bearing Age

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Fertility information is frequently a priority for young human papilloma virus (HPV) infected female patients, but provision of such information is often inadequate.

Women's sources of information about HPV extend beyond healthcare providers to include friends and family, health education classes, and the mass media, such as magazines, newspapers, radio, television, and books.

Given different motivating and constraining factors, presentation of HPV information varies considerably across information sources, leaving substantial informational gaps for clinicians to satisfy during patient visits healthcare providers should be prepared to discuss all explanations about HPV: transmission, prevention, detection, treatment.

Knowing that HPV is sexually transmitted, that transmission can occur through genital contact regardless of whether intercourse has taken place, and that condoms are not wholly protective against transmission.

With regard to progression, treatment, and risk of cancer, women wanted to know the typical duration of HPV infection, the nature of spontaneous resolution of the infection, the likelihood of developing cancer, and the screening and follow-up treatment that prevent most women from developing cancer.

In this study, we report our experience in counseling diagnosis and therapy of women with HPV infection. The accurate counseling demonstrated to be of high importance and efficacy.

Patients wanted to receive appropriate information on reproductive health and fertility even if they were not interested at the time of diagnosis.

## Impact of First Trimester Screening on Procedure Related Fetal Loss Rate among Women $\geq 35$ Years

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## BACKGROUND

According to Italian laws, maternal age  $\geq 35$  years represents one of the major indications for fetal karyotyping.

The aim of this study was to assess the impact of first trimester screening for Down's syndrome on procedure related fetal loss rate among women at 35 years or more.

## MATERIALS AND METHODS

Single center retrospective cohort study on singletons  $\geq 35$  years who underwent the first trimester screening for Down's syndrome over the last 10 years. First trimester screening was undertaken between 11 – 13 + 6 weeks' gestation by either combined screening or nuchal translucency (NT) alone. Nuchal translucency was performed by FMF certified operators. The number of cases with a risk lowered below 1:250 and the number of invasive procedure performed among the latter cases were calculated. A procedure related risk of 0.3% and a prevalence of abnormal karyotype of 0.5% were considered for the number of fetal loss avoided and karyotype abnormalities missed, respectively.

## RESULTS

Twenty-three thousand seven hundred and seventy-eight cases were included in the analysis. Nineteen thousand eight hundred and ninety-six (83.7%) cases showed a risk lower than 1/250 after the first trimester screening.

Among them, 9024 (45.4%) opted for fetal karyotyping regardless of the low risk at screening. Forty-five (0.5%) had an abnormal karyotype. Overall, 10872 procedures have been avoided. Thus, potentially leading to 32 fetal losses avoided and 54 fetal karyotype abnormalities missed.

## CONCLUSION

This study finding provide evidence that the first trimester screening among women at 35 or more years has the potential to reduce of 80% the access to fetal karyotyping in this subset of patients. However, almost half of the patient that showed a low risk after screening opted for fetal karyotyping anyway.

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# Developmental Programming of Cardiovascular Risk in Intrauterine Growth-Restricted Twin Fetuses According to Aortic Intima Thickness

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## OBJECTIVES

We aimed to test the hypothesis that aortic intima thickness is greater in intrauterine growth-restricted (IUGR) twin fetuses compared to normally developing twins, thus defining an increased cardiovascular risk that reflects genetic factors in fetuses sharing the same womb.

## MATERIALS AND METHODS

We conducted a prospective study performed on twins from January 2009 to July 2011. Twins were classified into three groups: IUGR fetuses with an estimated fetal weight below the 10th percentile and an umbilical artery pulsatility index of greater than 2 SDs (group A), fetuses with an estimated fetal weight below the 10th percentile and normal Doppler findings (group B), and fetuses with an estimated fetal weight appropriate for gestational age (group C). Aortic intima thickness was measured at a median gestational age of 32 weeks. Values were compared among groups and between each twin and cotwin, also considering sex and chorionicity.

## RESULTS

Twenty-five fetuses were classified as group A, 36 as group B, and 95 as group C. The median aortic intima thickness values were 0.9 mm in group A, 0.7 mm in group B, and 0.6 mm in group C ( $p < 0.0001$ ). There was a statistically significant difference between the aortic intima thickness of the twins and cotwins in groups A and B ( $p < 0.0001$ ). Sex and chorionicity did not correlate with aortic intima thickness.

## CONCLUSION

In this study, IUGR fetuses with Doppler abnormalities had greater aortic intima thickness, and IUGR twins with normal Doppler findings had intermediate thickness, supporting a genetic predisposition to cardiovascular risk independent of sex and chorionicity.

## Fetal Aortic Wall Thickness: A Marker of Hypertension in Intrauterine Growth-restricted Children?

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### ABSTRACT

Fetuses with intrauterine growth restriction (IUGR) have significant aortic intima-media thickening (aIMT), which suggests that preclinical atherosclerosis might predispose the infants to hypertension. However, the natural course of aIMT in babies with IUGR remains an open question.

The study enrolled 77 pregnant women between January 2007 and August 2009. The fetuses were classified as appropriate for gestational age (AGA) or IUGR, if the estimated fetal weight was between the 10th and 90th percentile or below the 10th percentile [with umbilical artery pulsatility index (PI) > SD], respectively. Anthropometric parameters and aIMT were detected in each IUGR and AGA fetus at a mean gestational age of 32 weeks. The follow-up was performed in 25 IUGR and 25 AGA infants at a mean postnatal age of 18 months; the previous measurements were repeated, and blood pressure measurements were taken. The maximum aIMT was significantly higher in the IUGR fetuses and infants compared with the AGA infants, both *in utero* ( $2.05 \pm 0.43$  vs  $1.05 \pm 0.19$  mm,  $p < 0.001$ ) and at the follow-up ( $2.3 \pm 0.8$  vs  $1.06 \pm 0.18$  mm,  $p < 0.0001$ ), the resulting values significantly correlated ( $p = 0.018$ ) with one another. The systolic blood pressure was significantly increased in the IUGR subjects ( $123 \pm 16$  vs  $104 \pm 8.5$  mm Hg,  $p < 0.0004$ ), and it correlated with the prenatal and postnatal aIMT values ( $p < 0.0156$  and  $p < 0.0054$ , respectively).

The aortic wall thickening progression in IUGR fetuses and infants differed from AGA, which may predispose the infants to hypertension early in life and cardiovascular risk later in life.

## First Trimester Combined Screening and Second Trimester Aorta Intima-media Thickness: Preliminary Data

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### BACKGROUND AND OBJECTIVE

First trimester combined screening data (nuchal translucency, free-beta-hCG, and PAPP-A) are known to be predictive of high-risk pregnancies. Aorta intima-media thickness (aIMT) values have been shown to be increased in IUGR fetuses resembling a sign of cardiovascular risk. The aim of this study was to analyze eventual correlations between first trimester combined screening data and second trimester aorta intima-media thickness.

### MATERIALS AND METHODS

Prospective study on singleton pregnancies: For the purpose of this study, we considered only normal pregnancies. We collected first trimester screening data to compare with second trimester aIMT.

### RESULTS

We analyzed 53 single pregnancies with regular course, mean woman's age was 31.58 years ( $\pm 4.24$ ), mean maternal BMI was  $22.97$  kg/m<sup>2</sup> ( $\pm 3.54$ ). Mean aIMT at 21 weeks was  $0.48$  mm ( $\pm 0.15$ ). Mean nuchal translucency in the first trimester was  $1.34$  mm ( $\pm 0.5$ ) (MoM  $0.84 \pm 0.23$ ), mean free-beta-hCG MoM was  $1.32$  ( $\pm 1.44$ ) and PAPP-A MoM was  $1.23$  ( $\pm 0.77$ ). Median gestational age at delivery was 39 weeks ( $\pm 1.38$ ) and median birth weight was  $3215$  gm ( $\pm 432$  gm). We confirm the increasing size of the aIMT with gestational weeks ( $p < 0.01$ ); even if there was not a significant correlation between nuchal translucency or PAPP-A and aIMT, a significant positive correlation between free-beta-hCG and aIMT was found ( $\rho = 0.336$ ,  $p < 0.05$ ).

### CONCLUSION

Biochemical free-beta-hCG testing before 12 weeks correlates with aIMT of the second trimester in normal pregnancies. Whether the association is also stronger in presence of IUGR requires further study.

## Conjoined Twins: Usefulness of Bi-Dimensional and Three-Dimensional Ultrasound in Prenatal Diagnosis: Two Case Reports

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### INTRODUCTION

Monochorionic monoamniotic twins are very rare, with an estimated incidence of 1% of monozygotic twinning.

Conjoined twins represent the rarest type of monozygotic, monochorionic, monoamniotic twins, with an approximate incidence of one in 50,000–100,000 births.

Conjoined twins are the result of incomplete separation of a single ovum, and the most accepted theory for their formation is incomplete splitting of a single embryo after the 13th day but before the 25th day after conception (Strauss et al 1987).

Conjoined twins are generally defined by the site of their most prominent union, which is ventral and dorsal in 87 and 13%, respectively. The abnormality is named with the suffix pagus, which means fixed. Types and distributions of ventral unions are cephalopagus (11%), thoracopagus (19%), omphalopagus (18%), ischiopagus (11%), and parapagus (pelvis and variable trunk; 28%), and types and distributions of dorsal unions are craniopagus (5%), as in our case, rachiopagus (vertebral column; 2%), and pygopagus (sacrum; 6%).

Ultrasound imaging is essential for prenatal diagnosis of conjoined twinning.

The chorionicity of the placenta can easily be determined in the first trimester, by two-dimensional (2D) ultrasound; with the application of the multiplanar capability of three-dimensional (3D) ultrasound, we were able to obtain an accurate depiction of the anomaly, playing an important role in the counseling and management of the patient.

### MATERIALS AND METHODS

We present a prenatal sonographic characterization of two interesting cases of conjoined twins, referred to our Fetal Medicine Unit, with the suspicion of 'pregnancy of Siamese twins': a case of dicephalus parapagus pregnancy, and a case of ischiopagus conjoined twins.

### RESULTS

Examination by 2D ultrasound demonstrated multiple anomalies and the site of conjunction in the winning pregnancies, contributing to define the form of Siamese twins: 'dicephalus parapagus' and 'ischiopagus' conjoined twins. Multiplanar 3D reconstruction techniques was essential to show the spatial arrangement of the fetal parts and undoubtedly useful in counseling and parenting prognostic formulation.

### CONCLUSION

An appropriate imaging strategy is a fundamental part of prenatal diagnosis of conjoined twins.

Three-dimensional allows an accurate characterization of complex anomalies in the conjoined twinning, and it may be more accurate than 2D sonography alone for defining an earlier diagnosis, the definite type of conjunction and organs shared between twins.

The clear images obtained with 3D ultrasound actually helped in counseling the parents and it is useful for a correct prognostic assessment and postnatal surgical treatment planning.

## First Trimester Nuchal Translucency Screening for Down's Syndrome: Single Center Experience on 100,000 Cases

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### BACKGROUND

Since its introduction in 1994, fetal nuchal translucency (NT) has changed prenatal screening for Down's syndrome. If only few centers accepted it in early days, nowadays it is used worldwide.

### MATERIALS AND METHODS

Single center retrospective cohort study on all singleton pregnancy that underwent NT for the first trimester screening for Down's syndrome. Nuchal translucency was measured between 11 + 0 and 13 + 6 weeks' gestation. Electronic ultrasound and pregnancy outcome databases were matched in order to assess the experience in NT over the last 22 years.



## RESULTS

One Lac cases were included in the analysis. Among these, 36.3% had a basal risk  $\geq 250$ . Nuchal translucency  $\geq 3.0$  mm in 1.5% of cases while fetal karyotyping was undertaken in the 12.4% of cases and showed an abnormal result in the 1.34% of cases. Nuchal translucency lowered the basal risk in the 92.3% of cases overall and in the 27.7% of women older than 35 years.

## CONCLUSION

These data confirm that NT has had a tremendous impact in the screening for Down's syndrome, lowering the need for fetal karyotyping and, consequently, the number of pregnancy losses following invasive prenatal testing.

## A New Technique for the Prenatal Ultrasound Evaluation of the Neurological Level of Lesion in Fetuses with Myelomeningocele

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It has been our concern to predict the future ability to walk, for fetuses with spina bifida, before birth. The MOMS trial has demonstrated the benefits of prenatal correction of myelomeningocele in comparison to expectant management. This study, though, has made no provision for the individual evaluation of motor function before birth, and the assumption has been made that the highest anatomical level of disruption can predict the functional neurological outcome.

Actually, functional segmental level of neurological lesion is the best known predictor for the ability to walk and the type of orthosis needed for ambulation. In patients with MMC, this is usually established after birth by the examination of voluntary and reflex movements in the lower extremities of the newborn. Inspiring on this postnatal examination, we have designed a system for the sonographic evaluation of lower-limb movements in fetuses with MMC, in an attempt to provide the prognosis for future ambulation before birth.

The segmental level is assigned according to that previously described by Sharrard in 1964, observing the most distal active muscles present by ultrasound (Table).

From March 2011 to April 2014, we evaluated 49 fetuses with MMC. After counseling, the parents opted for prenatal surgery, termination of pregnancy or expectant management. In our fetal medicine unit, patients undergoing prenatal surgery for MMC were periodically examined by ultrasound before birth and by a classical neurological clinical examination after birth. In the 11 fetuses operated before birth, included in our study, the agreement for the segmental levels assigned, between the prenatal ultrasound technique and the postnatal examination (gold standard) was 90.9% for the right limb ( $\kappa_w = 0.85$ ) and 81.8% for the left limb ( $\kappa_w = 0.80$ ). The fetuses maintained the neurological level stable after surgery and throughout the pregnancy.

In the assessment of spina bifida, the prognosis for walking ability is extremely important. Our experience in Vall d'Hebron suggests that prenatal assessment of neurological function in fetuses with MMC is feasible and may provide information about the ambulation prognosis for each patient evaluated. This could help the parents make better decisions regarding the pregnancy and could enable a better selection of candidates for prenatal correction of MMC.

**Table:** Metameric nerve level, key muscle groups, associated movements and walking prognosis

Level	Key muscle	Function	Ambulation prognosis
L1	Psoas	Hip flexion	Indoor ambulation with upper knee leg orthoses and crutches
L2	Hip adductor	Hip adduction	Similar to L1
L3	Quadriceps	Knee extension	Community ambulation with ankle foot orthoses $\pm$ crutches
L4	Hamstrings	Knee flexion	Community ambulation with ankle foot orthoses without crutches
L5	Tibialis anterior	Ankle dorsal flexion	Similar to L4
S1	Triceps/Soleus	Ankle plantar flexion	Community ambulation without orthoses

## Difficult Ultrasound Examination: How can Technology Help?

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## OBJECTIVES

Technically difficult patient (TDP) has physical characteristics that decrease the ultrasound waves ability to pass through anatomic structures; this particular condition creates images that are generally not sufficient to easily get the diagnosis with an high level of certainty. Maternal obesity is increasing and affects the quality of ultrasound images, but TDP are also women with peculiar structural characteristics: scars, strong abdominal muscles, oligohydramnios, polyhydramnios, twin pregnancies,

cosmetics creams. In this study, we evaluated which are the advantages of using new technologies in a group of obese pregnant women in the second trimester of pregnancy.

## MATERIALS AND METHODS

We used some of the new technologies of ultrasound imaging (Table on 10 patients with body mass index (BMI) > 30 during the second trimester ultrasound screening (GA 19-21 w). We evaluated: (A) image quality through subjective assessment of two operators (FT, GF), (B) time used to complete the scanning according to the second trimester scanning guidelines of the Società Italiana di Ecografia Ostetrica e Ginecologica (SIEOG), (C) need of exam repetition, (D) patient discomfort and (E) operator discomfort.

Table

- Spatial compounding
- Frequency compounding
- Harmonic imaging
- Broadband imaging
- Coded beamforming
- Speckle reduction algorithms
- High acoustic efficiency transducers
- New digital beamformers
- Transducers with very wide band

## CONCLUSION

The use of new technologies on TDP demonstrated a significant improvement in ultrasound imaging compared to traditional ultrasound imaging in terms of overall scanning quality, accuracy and suitability related to required standards. Furthermore, we found a decrease in scanning time, need for exam repetition, patient and operator discomfort.

## Distribution of Nuchal Translucency Values According to Fetal Condition: The Sinergic Effect

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## BACKGROUND

Increased nuchal translucency (NT) is a phenotypic expression of various fetal conditions, including chromosomal abnormalities and congenital heart disease (CHD).

Even if the NT increases the prevalence of fetuses affected by CHD, to date no study has compared the distribution of NT values among different fetal conditions. This study hypothesis is that different fetal conditions are related to different NT distributions.

## MATERIALS AND METHODS

Single center retrospective cohort study on all singletons pregnancies referred for the 1st trimester screening for Down's syndrome over the last 10 years. Four groups have been defined: (A) fetuses with trisomy 21 (T21) without CHD; (B) T21 and CHD; (C) abnormal karyotype (other than T21) without CHD, abnormal karyotype (other than T21) and CHD.

Nuchal translucency distributions were compared by Kernel density estimate and Kruskal-Wallis H test.

## RESULTS

Overall, 66870 pregnancies were included. Among these, 352 (0.5%) had T21; 66036 had normal NT or karyotype; 482 (0.7%) had other karyotype abnormality and 469 had a CHD. Prevalence of CD in the three subgroups were: 0.5, 22.7 and 15.4% for normal karyotype, T21 and other karyotype abnormality, respectively. Nuchal translucency distribution was significantly different between cases with T21 with and without CHD ( $p < 0.001$ ).

## CONCLUSION

The present study findings show that NT distribution varies according to fetal condition. Moreover, these data suggest a possible synergic effect of CHD and T21 on NT value.



## Conservative Treatment of Abnormally Invasive Placenta: A Case of Triple-P Procedure

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### INTRODUCTION

The incidence of morbidly adherent placenta has increased in the last decades, mirroring above all the increase in the rate of cesarean delivery. Significant maternal morbidity may occur because of massive postpartum hemorrhage, usually caused by the forced separation of adherent placenta from its underlying bed and surrounding structures. The traditional treatment of cesarean hysterectomy, associated with the severe complication of loss of fertility in young women, in selected cases can be successfully replaced by conservative techniques: uterine-sparing leaving the placenta *in situ* or Triple-P procedure. The second one consists in three steps: (1) Perioperative placental localization; (2) pelvic devascularization and (3) placental non-separation with myometrial excision and reconstruction of the uterine wall.

### CASE REPORT

A 29 years old gravida 2 para 1, affected by gestational hypertension and hypertransaminasemia, was admitted to our hospital at 28.0 weeks' gestation with the diagnosis of placenta previa major and suspected pre-eclampsia. Her obstetrical anamnesis consisted of one previous cesarean section. Admission ultrasonographic examination showed normal fetal biometry, normal Doppler flowmetry and anterior high placenta linked to a succenturiate cotyledon which covered the internal uterine orifice and presented intraparenchymal lacunae; the bladder line appeared irregular and the basal layer hypervascularized. These ultrasound signs were suggestive for focal accretism/incretism of the cotyledon. The patient was really motivated in preserving her uterus, above all because of her young age. She has been informed about the high risk of peripartum hemorrhage and the possibility of hysterectomy with ovarian conservation, if tightly necessary.

### MANAGEMENT

Cesarean delivery was performed at 36.1 weeks' gestation, after preoperative temporary occlusion of internal iliac arteries with balloon catheters by interventional radiologist. After Joel-Cohen incision, the anterior uterine wall appeared richly vascularized mainly in the lower uterine segment. We carried out a corporal transverse incision of uterine wall, in a zone without placental invasion, as previously evidenced by ultrasonography. After the delivery of an alive fetus and the administration of uterotonic agents, the whole placenta separated except the succenturiate cotyledon which was adherent. We resected a lozenge of uterine wall, area of the abnormal placental invasion and carried out an instrumental removal of placental residuals. In order to stabilize hemostasis, we made numerous hemostatic square sutures and practiced a B-Lynch suture. We reconstructed and sutured the anterior uterine wall. No postoperative complications occurred and the woman was discharged after 5 days.

### DISCUSSION

This case report supports the possibility of choosing a conservative treatment of abnormally invasive placenta, in order to preserve woman's fertility, if this is her preference. Preoperative diagnosis of placental localization and collaboration with interventional radiologist reduce the hemorrhagic risk. We exclude the Triple-P procedure in cases of placenta percreta with posterior and lateral parametrial invasion, but we suggest the possibility of execution in selected cases of placenta focally accreta/increta/percreta. For this reason, we underline the importance of diagnosis of placental invasion degree, for a correct management.

## Importance of Counseling and Ultrasound before Non-invasive Prenatal Testing: A Case Report

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A 37-year-old alloimmunized Rhesus disease (RhD) negative woman presented to our hospital for pregnancy monitoring at 12 weeks of gestation for 1st trimester risk assessment and RH isoimmunization.

In the current pregnancy, the presence of twins was first ascertained by ultrasonography at 6.6 weeks of gestation by the patient's obstetrician but the fact was not referred to us. A subsequent scan performed 1 week later by the same obstetrician revealed the absence of a beating fetal heart in one of the two embryos. At 12 weeks of gestation, the patient came to our obstetric and gynecology centre at Microcitemico Hospital for nuchal translucency (NT) and biochemical screening and genetic counseling. During the NT screening, our operator visualized only one fetus and the possibility of a vanishing twin was not considered since we were not informed about the initial visualization of twins by the patient's obstetrician.

In order to determine the fetal RhD status and sex of the ongoing pregnancy, at 14.2 weeks of gestation, the woman was offered a non-invasive prenatal testing (NIPT), for prenatal assessment of both RhD status and fetal sex, using the cell-free DNA isolated from maternal plasma.

The titer of the Rh antibodies was monitored throughout pregnancy by sampling maternal blood every 3 to 4 weeks from the 8th to the 30th week. The titers were consistently around 1:64 until the end of the pregnancy.

Quantitative real-time PCR was performed in the ABI Prism 7000 Sequence Detector System. Rhesus disease-gene analysis showed the consistent amplification of two exon 7 regions, deleted in the maternal genes, suggesting an RhD-positive phenotype of the surviving twin. This was supported by a positive Coombs test. During the ultrasound monitoring in our center performed at 14 weeks of gestation, we observed female fetal sex which was discordant from the NIPT results. Conversely, the fetal sex determination assays gave conflicting results, most likely influenced by the release of cfDNA from the vanishing twin, which presumably was a male fetus.

In the light of these results, it is important to emphasize the need for an accurate 1st trimester ultrasound monitoring of pregnancies and, above all, in the first several weeks of pregnancy in order to detect eventually the presence of vanishing twins, as well as the main role of pre- and post-test genetic counseling to clearly inform couples on pros and cons of NIPT, including, above all, the risk of incorrect result due to vanishing twin.

## Association between Fetal Atrioventricular Septal Defect and Chromosomal Abnormalities in the Current Era

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### OBJECTIVES

Atrioventricular septal defect (AVSD) constitutes an indication for fetal karyotyping, despite the existing risk of pregnancy loss related to invasive procedures. The aim of this study was to assess the rate of trisomy 21 in fetuses diagnosed with an AVSD in the era of first trimester screening and to ascertain if the rate differs according to first trimester risk for trisomy 21.

### MATERIALS AND METHODS

Fetuses diagnosed with an AVSD from 2002 to 2014 were retrospectively identified. The overall rate of trisomy 21 and other aneuploidies was calculated among cases with normal situs. The prevalence of trisomy 21 and other aneuploidies was also assessed in the subgroups of women with low and high first trimester risk for trisomy 21, using a cut-off risk value of 1:150.

### RESULTS

A total of 116 fetuses were identified. Atrioventricular septal defect was diagnosed at median gestation of 21 weeks (IQR: 17.6–22.4). Among 103 fetuses with normal situs, 72 fetuses had an isolated AVSD, and 31 fetuses had an AVSD associated with other abnormalities. The prevalence of trisomy 21 among fetuses with normal situs was 45% (95% CI: 35–54%). Within the low risk group, the rate was 41% (95% CI: 27–57%) while in the high risk group the rate was 67% (95% CI: 50–80%), significantly higher than in the low risk group ( $p = 0.036$ ).

### CONCLUSION

Despite first trimester combined screening, the rate of trisomy 21 among fetuses diagnosed with an AVSD in the second trimester remains high. Thus, advising for fetal karyotyping by invasive procedure is still a reasonable choice irrespective of pregnancy being identified as high risk or low risk group in the first trimester.

## Role of Oocyte Age on Early Fetal Growth

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### OBJECTIVE

To ascertain if embryos from assisted reproductive technology (ART) obtained with oocyte donation have different growth pattern at first trimester when compared to pregnancies from ART with homologous oocytes.



## MATERIALS AND METHODS

Retrospective study of consecutive pregnancies obtained by ART who underwent first trimester scan at a single tertiary referral center from 2010 to 2014. Exclusion criteria were: abnormal karyotype, fetal structural anomalies and monochorionic twin pregnancies. Pregnancies were dated according to date of oocyte aspiration. Crown-rump-length (CRL) and nuchal translucency (NT) were converted to centiles according to gestational age (GA) and CRL, respectively (Table). Recorded data regarding maternal age, oocyte age (defined as maternal age in homologous ART or donor age in heterologous ART), CRL centiles and NT > 95<sup>o</sup> centile were compared between three groups: homologous ART (group 1); oocyte donation (group 2); embryo donation (group 3).

## RESULTS

Seven hundred and ninety-one fetuses conceived with ART were included in the analysis: 652 (82.4%) in the group 1, 130 (16.4%) in the group 2, 9 (1.2%) in the group 3. The incidence of NT > 95th centile was not significantly different ( $p = 0.35$ ). On the converse, in group 1 CRL centiles were significantly lower than in groups 2 and 3 ( $p < 0.001$ ). Maternal age was significantly increased in groups 2 and 3 ( $p < 0.001$ ), while oocyte age was significantly lower ( $p < 0.001$ ). Linear regression was undertaken in order to ascertain the role of different parameters on fetal growth: a significant inverse correlation was found between CRL centile at first trimester scan and both oocyte age and maternal BMI, despite maternal or paternal age.

## CONCLUSION

Crown-rump-length centile at first trimester scan is significantly lower in pregnancies conceived by homologous ART compared to heterologous ones. This study showed a linear inverse correlation between CRL centile at first trimester and both oocyte age and maternal body mass index (BMI). A possible role of oxidative stress on early embryonic growth should be considered.

**Table:** Linear regression analysis exploring correlation between oocyte age and CRL centile at first trimester scan

	<i>Beta</i>	<i>95% CI</i>	<i>95% CI</i>	<i>p-value</i>
Oocyte age	-0.13	-0.68	-0.08	0.01
Male age	0.09	-0.06	0.62	0.11
Maternal BMI	-0.11	-1.20	-0.03	0.04
Smoke	0.03	-6.33	12.00	0.54
Oocyte cryopreservation	0.02	-14.26	20.67	0.72

## Cryopreservation of Ovarian Tissue in Neoplastic Patients at High Risk of Premature Ovarian Failure: A Single Center Experience

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According to the Institute for Health, every year in Italy, and there are about 250,000 new cases of tumor, 8000 affect patients younger than 40 years of whom 5000 are women. During the last decades, the prognosis for such patients has improved revealing the side-effects of anti-neoplastic therapies. Meanwhile in developed countries, maternal age at first pregnancy has reached 35 years increasing the proportion of neoplastic patients with unsatisfied parity.

Thus, this has led to an increasing interest on ovarian tissue cryopreservation for neoplastic women.

To date, the options for fertility preservation before anti-neoplastic therapies are represented by: ovarian transposition, administration of GnRH analogues during gonadotoxic therapy, cryopreservation of mature oocytes, embryo cryopreservation and cryopreservation ovarian tissue.

To date, the latter option seems the most promising, even if considered experimental. It should also be noted that in Italy, in accordance with the law 40/2004, embryo cryopreservation is considered illegal. On the other hand, oocyte cryopreservation has the main limitation in the need for ovarian stimulation, which is contraindicated in the vast majority of tumors, inapplicable to prepubescent patients and that results in a 2 weeks delay in starting anti-neoplastic therapies.

The use of GnRH analogues is not shared by the entire scientific community, the guidelines of American Society Clinical Oncology (ASCO) consider it a little strategy supported by scientific evidence.

From March 2014 to date, at the Center for Medically Assisted Procreation Hospital Microcitemico, Cagliari it has been taken over six patients, aged between 12 and 36 years. Of these two did not undertake ovarian tissue cryopreservation: one woman was excluded because referred after four cycles of chemotherapy and with undetectable anti-Müllerian hormone; the other, 36 years old suffering from rectal cancer, declined for personal decision.

The four cases treated involved a 12-year-old girl with ovarian teratoma, a 35-year-old woman suffering from breast cancer, a 25-year-old girl suffering from Hodgkin's disease and a 18-year-old girl suffering from medulloblastoma.

## Biometry of Fetal Cortical Development by 3D Ultrasound

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### OBJECTIVES

The aim of this study was to measure the depth of parieto-occipital fissure, calcarine sulcus, insula and Sylvian fissure of the fetal brain in order to establish normal reference ranges. Furthermore, to find out whether there are gender related structural brain differences and left-right differences between the brain hemispheres.

### MATERIALS AND METHODS

In a cross-sectional study, three-dimensional (3D) ultrasound volumes of fetal brains were acquired from axial, coronal and sagittal planes. All scans were performed using E8 General Electric equipment (Zipf, Austria), with a 5 to 8 MHz 3D transabdominal or 5 to 9 MHz 3D transvaginal transducer. Depth of parieto-occipital sulcus, calcarine sulcus, insula and Sylvian fissure was measured in the axial and coronal plane to find out the differences in the cortical development throughout gestation. Furthermore five cases with brain pathologies (two with arachnoidal cyst one with brain hemorrhagia and two with partial corpus callosum agenesis) were studied in order to show the clinical relevance of the new reference ranges.

### RESULTS

Over a period of 4 years, 514 normal fetuses between 13 and 40 gestational weeks were examined. The volumes were acquired in 311 cases by transvaginal and in 201 cases by transabdominal ultrasound.

The comparison of brains in male and female fetuses did not reveal striking differences. Concerning differences between the left and right hemisphere we could find out that the parieto-occipital fissure shows a higher depth on the left side.

### CONCLUSION

Fetal brain development follows a predictable time table. Knowledge of appearance and degree of morphological changes may help in the detection of fetal brain pathology. In contrast to 2D ultrasound 3D sonography enables a precise evaluation of the fetal cortical development.

## Reproductive Issues in Women with $\beta$ -Thalassemia Major

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The  $\beta$ -thalassemia is an autosomal recessive genetic syndrome, caused by point mutations or, less frequently, by gene deletions that lead to reduced or absent  $\beta$ -globin chain synthesis. The majority of homozygotes are affected by  $\beta$ -thalassemia major, which entails severe anemia and imposes the need for a blood transfusion. Sometimes even homozygous for a mutation does not require transfusions (i.e. thalassemia intermedia).

The blood transfusion regimen in which the patients are subjected from birth implies, despite the association of chelating agents, an important iron accumulation in the liver, the pancreas, the heart and in pituitary glands. In particular, the suffering of pituitary parenchyma involves late menarche and primary or secondary amenorrhea.

However, because of the therapeutic advances in recent decades, life expectancy has considerably increased, resulting in a growing desire for motherhood by women  $\beta$ -thalassemia and in a raised interest on issues related to the induction of ovulation and pregnancy in these patients.

Until the eighties, the cases of pregnancy in thalassemia patients were sporadic, while in recent years the number has increased considerably, although ovarian stimulation is often due to the dysfunction of the hypothalamic-pituitary-gonads axis.

In the regional center for microcitemie, during the last 10 years of clinical activities; we subjected to a treatment of medically assisted procreation 22 patients with  $\beta$ -thalassemia major; four patients were performed 14 cycles of ovulation induction associated with targeted reports, 14 patients in 37 cycles of ovulation induction associated with intrauterine insemination while in 11 patients were performed 21 cycles of ovulation induction associated with fertilization vitro.

Twenty pregnancies were obtained with evolutionary birth of 19 children.

In this subset of patients the stimulation protocol, the doses of exogenous gonadotropins, clinical and ultrasound monitoring should be customized in order to reduce the risk for hyperstimulation syndrome and multiple pregnancy.



In thalassaemic woman, before facing an ovulation induction treatment, it is important to consider the overall condition of the patient, to choose the most appropriate time. In fact, in addition to issues related to the obtaining of pregnancy, it is then to consider those related to its evolution.

## CONCLUSION

The achievement of pregnancy in women with  $\beta$ -thalassaemia is a possible event and increasingly rare, thanks to advances in conventional therapy (blood transfusion and chelation) and knowledge in the pathophysiology of reproduction. However, the possibility of the occurrence of serious complications in the mother and the fetus makes imperative a careful baseline assessment of patient and careful monitoring providing for close collaboration between gynecologist and teams who routinely charge the patient.

## Ultrasound Long-term Follow-up of Residual Postpartum Trophoblastic Tissue

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## AIM

Long-term ultrasonic evaluation of uterine cavity changes in conservatively treated patients with mild secondary postpartum hemorrhage caused by residual trophoblastic tissue.

## MATERIALS AND METHODS

Two-dimensional and three-dimensional transvaginal sonography combined with color Doppler evaluation was performed in three patients who were presented with secondary postpartum hemorrhage. For all patients, management was conservative without drug usage or uterine evacuation and all women were discharged but reattended our department for ultrasound surveillance. The ultrasound assessments were repeated according to the clinician's judgement in the time period of 1 to 2 weeks after the first examination to the intervals of few months in the long-term follow-up.

## RESULTS

Initial sonographic examination revealed typical finding for residual trophoblastic tissue showing uterus with hyperhypoechoic/hyperechoic masses accompanied with low-resistance Doppler indices. Long-term ultrasound follow-up revealed involution process of the uterus with regression and degeneration of intracavitary masses.

## CONCLUSION

This report supports the opinion that the patients with postpartum residual trophoblastic tissue can be treated conservatively with repeated ultrasonographic evaluation. This management avoids potentially hazardous surgical treatment, but enables instant action if necessary.

## Preimplantation Genetic Diagnosis for Mendelian Genetic Diseases: Sardinian Experience

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The thalassemiias are an heterogeneous group of autosomal recessive disorders characterized by reduced or absent production of  $\beta$ -globin chain, condition caused by mutation in the  $\beta$ -globin gene; the clinical picture of the homozygous state or compound heterozygous is characterized by severe anemia, requiring regular blood transfusion, with iron chelation therapy, spleen and liver expansion and bone modification.

In Sardinia, an Italian island in the Mediterranean Sea with a 1,700,000 inhabitants the incidence of  $\beta$ -thalassaemia carriers is estimated around 13% and one couple in 60 is at risk of having an affected child.

Our program of prevention and control of the disease is based on the accurate diagnosis of carriers, genetic counseling and prenatal diagnosis.

At present time, prenatal diagnosis is widely applied and amongst the patients we have found an acceptability of 93.2% for fetal blood sampling, 96.4% for amniocentesis and 99.3% for chorionic villus sampling. This behavior demonstrates how the technique acceptability depends on the precocity of the procedure.

Although traditional prenatal diagnosis has reduced the number of newborns affected by thalassemia, therapeutic abortion is not eliminated in case where an affected fetus is diagnosed and from 1977 to 2002 a total of 6,000 invasive prenatal diagnosis have been performed (1,164 diagnosis by Fetal Blood Sampling, then 203 diagnosis by Amniocentesis and since 1984, 4,633 diagnosis by Chorionic Villus Sampling); 1,505 patients have had a genetic result of affected fetus, and all, except 18 patients, opted for the interruption of the pregnancy with notable psychological and physical traumas.

Preimplantation genetic diagnosis has been introduced in our department as an alternative to prenatal diagnosis in order to prevent affected pregnancies in couples who are carrier for monogenic diseases.

In this study, we report our experience in preimplantation Genetic Diagnosis accomplished by the biopsy of one or two blastomeres from cleavage stage embryos before 2004 and after 2014.

Between January 2001 and 2004 (before the 40/2004 law) 23 couples have been included in the PGD program with a total of 42 cycles performed.

A total of 98 embryos were identified as unaffected of which 75 embryos were transferred in 31 cycles. In the infertile patient group, two biochemical pregnancies (11.1% per transfer), in the fertile patient group four clinical pregnancies (30.8% per transfer) were obtained.

Between October 2013 to April 2015 (post restriction of the 40/2004 Italian law) 32 couples have been included in the PGD program for monogenic disease with a total of 52 cycles and 40 ET performed. Four biochemical pregnancies (10% per transfer), 1 miscarriage (4.0% per transfer), 8 clinical pregnancies (20% per transfer) were obtained.

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## **Surgically Correctable Congenital Fetal Anomalies: Ultrasound Diagnosis and Management**

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Great number of long-life disabilities are due to the congenital malformations. Evolution of prenatal ultrasound diagnosis and improvement of surgical technique enabled us to detect most of these malformations *in utero* early and accurately with a possibility of early surgical management in selected cases even *in utero*. Advances in pre/perinatal management enabled us to interfere and change the origin of the disease in order to optimize the best postsurgical outcome. Only multidisciplinary team of specialist could provide such appropriate treatment.