Postmortem examination of human fetuses: a comparison of 2-dimensional ultrasound with invasive autopsy

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Abstract

Objective: To compare the diagnostic usefulness of postmortem ultrasound with invasive autopsy in fetuses at different gestational ages.

Methods: We performed postmortem 2-dimensional ultrasound on 163 fetuses at 13-42 weeks gestation, blinded to clinical details. Logistic regression analysis was used to investigate the effect on non-diagnostic results of gestational age during postmortem ultrasound, presence of maceration, and cause of death. In 123 cases

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where invasive autopsy was available, the diagnostic accuracy of ultrasound in detecting major organ abnormalities was evaluated, using invasive autopsy as a gold standard.

Results: For the fetal brain, a non-diagnostic result was found in 17 (39.5%) of 43 fetuses with maceration and was significantly more common as compared to fetuses without maceration (24 [20.0%] of 120 fetuses [p=0.013]). For the fetal thorax, a non-diagnostic result was found in 15 (34.1%) of 44 fetuses at <20 weeks of gestation and in 13 (10.9%) of 119 fetuses at ≥20 weeks (p<0.001). For the heart and abdominal organs no association was demonstrated with the tested variables. For fetuses <20 weeks, specificity was 83.3% for brain anomalies, 68.6% for the thorax, and 77.4% for the heart. For fetuses ≥20 weeks, sensitivity and specificity were, respectively, 61.9% and 74.2% for the brain, 29.5% and 87.0% for the thorax, and 57.1% and 76.9% for the heart. Sensitivity was 60.7% and specificity 75.8% for fetal abdominal organs, mainly the kidneys, irrespective of gestational age.

Conclusion: Although maceration may lead to failure in some cases, postmortem ultrasound reaches diagnostically acceptable levels for brain and abdominal organs, compared with conventional autopsy. It may therefore play a role as a first-line examination before other virtual autopsy techniques are indicated.

Introduction

Following termination of pregnancy (TOP), it is widely acknowledged that postmortem examination is important not only to confirm prenatal findings, and therefore to assess clinical practice, but also to help counsel parents concerning the recurrence rate for future pregnancies[1-5]. While perinatal autopsy rates are declining, the last decade has witnessed the emergence of alternative techniques, such as virtual autopsy, mainly using magnetic resonance imaging (MRI)[6-18].

Virtual autopsy techniques are significantly more acceptable to parents than conventional invasive techniques[12,19], and in some instances, postmortem MRI may have a higher success rate than conventional autopsy, particularly for the developing fetal brain [9,12,14].

Among postmortem imaging techniques, postmortem ultrasound (US) has not been assessed in detail. It is a widely available, cheap technique and could potentially be used by fetal medicine specialists as a first-line examination before other techniques are indicated.

Historically, the first study describing the use of US for postmortem examination is the one by Fariña et al. however it did not concern fetuses[20]. Only one study has thus far reported the feasibility of postmortem US, in a series of 88 fetuses at 11-40 weeks gestation (unpublished data). Abnormality detection rates were 91.6% for the brain, 92.8% for the thorax including the heart, and 85.7% for the abdominal organs. Respective specificities were 90.7%, 92.8%, and 94.5%, although the study was not powered strongly, and the reported confidence intervals were wide with this number of subjects. The generalizability of this study is also limited as all examinations were performed by a single operator who was aware of all prenatal findings (unpublished data), but allow us to infer feasibility of the technique. The technique should clearly be comprehensively evaluated in a larger cohort of subjects.

Our aim was to study the diagnostic accuracy of postmortem US performed by experienced operators blinded to the prenatal and the conventional autopsy results.

Material and Methods

Study participants and design

This was a prospective multicentre study, conducted at the Fetal Medicine Unit of the University Hospital Brugmann, Université Libre de Bruxelles, Brussels, Belgium and Great Ormond Street Hospital for Children NHS Foundation Trust, London, UK. Each local ethics committee approved the study. Between January 2014 and December 2016, postmortem US was offered to all parents following TOP, in utero fetal death (IUFD), or miscarriage, in addition to conventional autopsy or minimally invasive autopsy (MIA) with endoscopic postmortem examination. All fetuses were delivered vaginally following induction of labor. Dilation and Curettage was not performed in any of the fetuses included in this study. Postmortem US was offered alongside existing clinical service provision of full autopsy or MIA. Parental consent was obtained for postmortem US, MIA, and conventional autopsy. Fetuses were stored in refrigerated compartments at 4°C before postmortem US examination.

Postmortem US

Postmortem 2-dimensional US was performed by fetal medicine specialists or paediatric radiologists, all with more than 5 years' experience in prenatal imaging. Examinations were performed using a Voluson E8 (GE Medical Systems, Zipf, Austria) machine, equipped with transducers or a LOGIQ E9 machine (GE Healthcare, Chalfont St Giles, England) using high frequency probes.

Operators performing postmortem US were blinded to antenatal imaging and any subsequent clinical findings, but were given the gestational age and mode of death (TOP, IUFD, miscarriage). To ensure conformity with the protocol, none of these operators were involved, at any stage, in the prenatal care of the fetuses they had to scan.

Nineteen internal organs were analyzed and described as diagnostic (normal, abnormal), or non-diagnostic depending on whether the organ could be seen and distinguished clearly for diagnosis. They were then grouped into 4 anatomic regions: brain (corpus callosum, thalamus, cerebral ventricles, cortex, and cerebellum), thorax (thymus, trachea, and lungs), heart (heart ventricles, atria, septum, and great arteries), and abdomen (liver, spleen, stomach, adrenals, kidneys, bladder, and bowels). Since clinical examination and skeletal radiography provide excellent performance in the diagnosis for musculoskeletal system, we simply listed anomalies of the musculoskeletal system, without analyzing accuracy of postmortem US. The anatomic region was considered normal when every organ within it was normal, or abnormal if at least one organ was abnormal; and non-diagnostic when at least one organ was non-diagnostic and the others were normal. The results were entered into an independent database immediately after postmortem US examination and before conventional autopsy, if this was requested.

Conventional postmortem examination and MIA

Conventional autopsy or MIA was performed by specialist perinatal / paediatric pathologists with more than 15 years of experience in fetal autopsy, according to national guidelines, which includes microscopic evaluation.

MIA by endoscopic postmortem examination was performed according to a previously described method[21].

The pathologists were informed of the main prenatal findings related to fetal death in order to produce a full clinical report for future parental counseling. They were blinded to the postmortem US results. The descriptions of the previously listed 19 organs were selected and grouped as previously described for future comparison.

Fetal maceration was determined on macroscopic examination. We decided that effective maceration was present when more than 10% of fetal skin was detached or when internal organs showed significant autolysis. A conventional autopsy was described as non-diagnostic for an organ when a complete dissection was impossible to obtain due to important autolysis.

Statistical analysis

Logistic regression analysis was used to investigate the effect on non-diagnostic results of gestational age during postmortem US (<20 weeks, ≥ 20 weeks), presence of maceration (yes, no), and cause of death (TOP, IUFD, miscarriage), as categorical variables.

Sensitivity and specificity and their 95% confidence intervals were calculated. We included the non-diagnostic cases in the group of false negatives for calculation of sensitivity and in the group of false positives for calculation of specificity. Concordance was defined as the sum of true positives and true negatives divided by all cases including non-diagnostic cases. Discordance was defined as the sum of false negatives and false positives divided by all cases including non-diagnostic cases. Sensitivity, specificity, concordance and discordance rates, and non-diagnostic rate for the overall organs were compared between fetuses <20 weeks and fetuses ≥20 weeks, using Fisher's exact test.

Data are presented as medians unless stated otherwise. Data were analyzed with the statistical software SPSS version 23.0 (SPSS Inc., Chicago, IL, USA), R version 3.0.2 (The R Foundation for Statistical Computing, Vienna, Austria) and Excel version 9.0 (Microsoft, Redmond, WA, USA). A two-sided $P<0.05$ was considered to be statistically significant.

Results

Gestational age ranged from 13 to 42 (median 23) weeks in the 163 cases included (Fig 1). Postmortem US was performed 0 to 39 (median 2) days after delivery. Conventional autopsy was performed in 112 cases and 11 cases underwent MIA in this dataset, at a range of 0 to 47 (median 5) days after delivery. In these 123 cases, 95 had brain autopsy. Gestational age at delivery was <20 weeks in 35 and ≥20 weeks in 77. Seventy-six fetuses had at least one anomaly confirmed at autopsy or MIA. These anomalies are listed in Table 1.

For the fetal brain, postmortem US was diagnostic in 122 (74.8%) of 163 fetuses. A non-diagnostic result was found in 17 (39.5%) of 43 fetuses with maceration and in 24 (20.0%) of 120 fetuses without maceration. Univariate regression analysis showed that a non-diagnostic result was significantly more common when associated with maceration, but not with gestational age during postmortem US or with cause of death (Table 2).

For the fetal thorax excluding the heart, postmortem US was diagnostic in 135 (82.8%) of 163 fetuses. A non-diagnostic result was found in 15 (34.1%) of 44 fetuses at <20 weeks gestation and in 13 (10.9%) of 119 fetuses at ≥20 weeks. Univariate regression analysis showed that a non-diagnostic result was significantly more common for gestational age <20 weeks as compared with ≥20 weeks, but was not associated with maceration or cause of death.

For the heart postmortem US was diagnostic in 134 (82.2%) and for abdominal organs in 132 (81.0%) of 163 fetuses. For both anatomic regions, we found no association between the rate of non-diagnostic results and gestational age, the presence of maceration, or the cause of death (Table 2).

Accuracy analysis showed that postmortem US of all organs had a sensitivity of 74.7% (95% CI 64.8-84.5) and a specificity of 83.3% (95% CI 70.0-92.5), with a concordance rate of 78.0 % (95% CI 70.7-85.4) and a discordance rate of 6.5 % (95% CI 3.3-12.3) (Table 3). Overall, no significant difference was found between the fetuses of gestational age <20 weeks and ≥20 weeks.

Accuracy analysis of postmortem US for fetuses <20 weeks gestation

For the fetal brain and thorax, too few cases with abnormalities were available for the calculation of sensitivity. Specificity was 83.3% for the brain and 68.6% for the thorax. For the fetal heart, none of the 6 abnormalities were diagnosed and specificity was 77.4%. Finally, for the fetal abdomen, sensitivity was 71.4% and specificity 73.3% (Fig 2 and Table 3).

Accuracy analysis of postmortem US for fetuses ≥20 weeks gestation

For the fetal brain, sensitivity was 61.9% and specificity 74.2% for detecting anomalies (Table 3). Fetuses with agenesis of the corpus callosum, ventriculomegaly, calcification due to congenital toxoplasmosis, or lesions due to tuberous sclerosis were diagnosed (Fig 3, 4). Abnormalities of gyration were missed on postmortem US (Table 1).

For the fetal thorax, sensitivity was 29.5% and specificity 87.0% (Table 3). The majority of missed diagnoses concerned abnormal lung lobulation. The diagnosis was missed in one case of right-sided congenital diaphragmatic hernia at 23 weeks and 2 days associated with exomphalos (Table 1).

For the fetal heart, sensitivity was 65.0% and specificity 83.1% (Table 3). Postmortem US was better at diagnosing anomalies seen in the 4-chamber view than of the great vessels (Table 1).

For the fetal abdomen, sensitivity was 57.1% and specificity 76.9% (Table 3). Postmortem US was mainly useful for detecting anomalies of the kidney (Fig 5-8) (Table 1).

Only minor differences were found in the detection of skeletal anomalies, more details of which are provided in Table 1.

Discussion

Main findings

Our study found that postmortem US had overall diagnostic accuracy of 74.7% sensitivity and 83.3% specificity. We also found that non-diagnostic rates were higher in those in whom the brain was macerated, and in younger gestation fetuses <20 weeks for the thorax and heart. Nevertheless, postmortem US was diagnostic in 74.8% of fetuses for the brain and more than 80% for the rest of the body. Postmortem US as compared with conventional autopsy reaches diagnostically acceptable levels for brain and abdominal organs, but is less accurate for thoracic, mainly heart, structures.

Comparison with previous studies

Votino *et al.* evaluated the feasibility of postmortem US as a virtual autopsy technique in 88 fetuses at 11-40 weeks gestation (unpublished data). A postmortem US examination was possible in 95% of the fetuses, and sensitivity and specificity of detecting abnormalities was about 90%, irrespective of the organ that was evaluated and of gestational age at evaluation. In our study, the rate of non-diagnostic results was about three times higher and detection rate of abnormalities was significantly lower (especially for the heart). Whilst one explanation is a higher number of early gestation fetuses in our study, this is unlikely as 50% of Votino et al's cases were < 20 weeks gestation. A more likely explanation is that we had multiple operators across a range of clinical scenarios, who were blinded to the antenatal imaging, compared to a single unblinded operator, which makes our results more clinically relevant.

In the last decade, the most studied virtual autopsy technique is that based on postmortem MRI at 1.5-T [6-12, 14-18]. Although diagnostic performance is better for postmortem MRI [18], the non-diagnostic rate for fetuses < 20 weeks gestation using postmortem MR was 53.8% but only 24.3% with postmortem US in our study. The overall specificity for different organs was better using postmortem US than postmortem MRI and sensitivity and specificity were somewhat better for abdominal organs, although a formal statistical evaluation and direct comparison in the same patients has not been performed.

Implications for practice

With the decline of conventional autopsy rates following TOP, any alternative postmortem examination is better than no examination.[12] However, even in cases where parents give consent our present study shows that 20% of brain anomalies are non-diagnostic at conventional postmortem, a rate similar to the 18% with postmortem US. In a previous study, virtual autopsy using 1.5-T MRI yielded a diagnostic result in 82% of 39 fetuses with non-diagnostic results on conventional autopsy[18]. Furthermore, conventional 1.5-T MRI of the fetal brain has been widely studied and is quite effective in detecting abnormalities in fetuses of gestational age above 20 weeks. We conclude that the data currently supports the preferential use of postmortem MRI rather than postmortem US above 20 weeks gestation for the fetal brain.

For the fetal heart after 20 weeks gestation, while postmortem US may be acceptable for major anomalies seen in the 4-chamber view, it remains very poor for evaluating the great vessels. However, conventional 1.5-T MRI is equally poor and more advanced techniques, such as MRI at 9.4-T or micro-CT, are unlikely to be successful due to the large size of fetuses during the second half of pregnancy [22,23].

Preliminary data show a 20 % improvement of the overall concordance rate with conventional autopsy of heart abnormalities using 3.0-T as compared to 1.5-T MRI[18].

For the fetal thorax after 20 weeks gestation, lung parenchymal anomalies were under-represented in our study, with about half of the cases concerning lung lobulation, with fewer anomalies of lung than of other organ groups. As a consequence, we cannot draw conclusions for this specific indication, although abnormalities of lung lobation may have limited clinical consequences.

Finally, postmortem US has high success rate and performance irrespective of gestational age for the fetal abdomen, and thus is a promising technique for the fetal kidney and could potentially be proposed as an alternative to MRI. Further, histological examination of the kidneys might be important and so the opportunity to evaluate postmortem US-guided percutaneous biopsies is now appealing.

With regard to the group of fetuses examined before 20 weeks gestation, postmortem US seems to be promising for the brain and thorax, in terms of success rate and specificity, but the number of anomalies were too small to evaluate their detection rate. Given that alternative techniques such as MRI at 9.4-T or micro-CT are not widely available, postmortem US may be considered acceptable as a first-line examination. Unfortunately, our results for the heart are quite disappointing, since none of the 6 anomalies were diagnosed.

Study limitations

Our study has some limitations. Firstly, some clinical scenarios will be under-represented and thus definitive conclusions cannot be drawn, particularly about fetuses below 16 weeks. We also recognize that postmortem US was performed in a tertiary referral setting and may not be representative of how this may be adopted into clinical services. Secondly, we did not compare the performance of postmortem US and MRI in the same fetuses, and clearly a formal comparison is needed. Thirdly, we did not evaluate the effect of operator experience, inter-individual nor intra-individual variability, nor the performance of fetal medicine specialists against pediatric radiologists. It may be that increased training in a specific area (e.g. fetal cardiac scanning or brain sonography) would increase postmortem diagnostic accuracy. However, our results reflect every day practice and thus are more generalizable.

Conclusions

Postmortem US has acceptable diagnostic accuracy for the fetal brain and abdomen, but is limited in younger gestation or macerated fetuses. As postmortem US is cheap, widely available and therefore quite attractive as a virtual autopsy technique, it may have a role as a first line examination in younger gestation fetuses where other imaging techniques struggle, although specific imaging of the heart remains problematic. Further studies are needed to establish its diagnostic accuracy in a direct comparison against other imaging techniques, rather than just postmortem.

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Table 1. List of confirmed abnormalities identified at autopsy/minimally invasive autopsy as compared with the results of abnormalities identified at postmortem US.

Abnormalities	Autopsy/ minimally invasive autopsy	Postmortem US			
		Same diagnosis	Abnormal organ but different diagnosis	Normal organ	ND
Brain (n=21)					
Agenesis of the corpus callosum	6	6	0	0	0
Brain hemorrhage	1	0	0	0	1
Brain tumor	2	1	0	1	0
Bronchopulmonary foregut malformation	1	0	0	1	0
Lesions due to congenital cytomegalovirus	1	0	0	0	1
Lesions due to congenital toxoplasmosis	1	1	0	0	0
Polygyria	2	0	0	1	1
Porencephaly	1	0	1	0	0
Ventriculomegaly/hydrocephaly	5	4	0	1	0
Neural tube defect	1	1	0	0	0
Thorax excluding heart (n=9)					
Abnormal lung lobulation	5	0	0	4	0
Diaphragmatic hernia	2	1	0	1	0
Thymic agenesis	2	1	0	0	1
Heart (n=27)					
Atrial septal defect	2	0	0	1	1
Atresia/stenosis of the pulmonary artery	3	1	0	0	2
Atrio-ventricular septal defect	2	0	0	2	0
Coarctation of aorta/aortic interruption	2	0	1	1	0
Complex congenital heart	3	2	0	0	1
Dilated heart	2	0	0	2	0
Double outlet right ventricle	1	0	1	0	0
Hypoplastic aorta	1	0	0	1	0
Rhabdomyoma	3	3	0	0	0
Tetralogy of Fallot	2	0	1	0	1
Transposition of the great vessels	2	0	0	1	1
Truncus arteriosus	1	1	0	0	0
Ventricular septal defect	3	1	0	0	1
Abdomen (n=23)					
Absent kidney	1	1	0	0	0
Anal atresia	3	0	2	1	1
Cystic dysplastic kidney	6	5	1	0	0
Ectopic kidney	1	1	0	0	0
Exomphalos	2	1	1	0	0
Hepatosplenomegaly	1	0	0	1	0
Intestinal malrotation	2	0	0	1	1
Multiple spleen	3	0	0	3	0
Obstructive uropathy	1	1	0	0	0
Pelvic kidney	1	0	0	1	0
Small kidney	1	0	0	1	0
Uterus unicornus	1	0	0	1	0
Skeleton (n=24)					
Abnormal number of vertebrae	1	0	0	1	0
Finger abnormalities (small)	4	0	0	4	0
Hemi-vertebrae	1	0	0	1	0
Limb abnormalities	9	8	0	1	0
Skeletal dysplasia	9	7	1	1	0
Other (n=11)					
Cleft	4	1	0	3	0
Craniosynostosis	2	2	0	0	0
Hydrops	3	3	0	0	0
Hypospadias	1	0	0	1	0
Limb body wall complex	1	1	0	0	0

Table 2. Logistic regression analysis in the prediction of factors leading to a non-diagnostic results during postmortem ultrasound (n=163).

Variable	Total number of fetuses (%)	Number of fetuses with non-diagnostic result (%)	Univariate analysis	
			Odds ratio (95% CI)	p
Brain		41 (25.2)		
Gestational age				
< 20 weeks	44 (27.0)	15 (34.1)	1.850 (0.865-3.956)	0.113
≥ 20 weeks	119 (73.0)	26 (21.8)	1	
Maceration				
Yes	43 (26.4)	17 (39.5)	2.615 (1.226-5.579)	0.013
No	120 (73.6)	24 (20.0)	1	
Cause of death			1.362 (0.878-2.113)	0.168
TOP	82 (50.3)	13 (15.9)		
IUFD	47 (28.8)	21 (44.7)		
Miscarriage	34 (20.9)	7 (20.6)		
Thorax excluding heart		28 (17.2)		
Gestational age				
< 20 weeks	44 (27.0)	15 (34.1)	4.218 (1.805-9.855)	<0.001
≥ 20 weeks	119 (73.0)	13 (10.9)	1	
Maceration				
Yes	43 (26.4)	6 (14.0)	0.722 (0.272-1.922)	0.515
No	120 (73.6)	22 (18.3)	1	
Cause of death			1.417 (0.860-2.337)	0.172
TOP	82 (50.3)	12 (14.6)		
IUFD	47 (28.8)	7 (14.9)		
Miscarriage	34 (20.9)	9 (26.5)		
Heart		29 (17.8)		
Gestational age				
< 20 weeks	44 (27.0)	12 (27.3)	2.250 (0.972-5.206)	0.058
≥ 20 weeks	119 (73.0)	17 (14.3)	1	
Maceration				
Yes	43 (26.4)	8 (18.6)	1.078 (0.438-2.653)	0.871
No	120 (73.6)	21(17.5)	1	
Cause of death			1.525 (0.931-2.497)	0.094
TOP	82 (50.3)	12 (14.6)		
IUFD	47 (28.8)	7 (14.9)		
Miscarriage	34 (20.9)	10 (29.4)		
Abdomen		31 (19.0)		
Gestational age				
< 20 weeks	44 (27.0)	10 (22.7)	1.373 (0.588-3.205)	0.464
≥ 20 weeks	119 (73.0)	21 (17.6)	1	
Maceration				
Yes	43 (26.4)	8 (18.6)	0.964 (0.395-2.353)	0.936
No	120 (73.6)	23 (19.2)	1	
Cause of death			1.215 (0.748-1.973)	0.431
TOP	82 (50.3)	13 (15.9)		
IUFD	47 (28.8)	11 (23.4)		
Miscarriage	34 (20.9)	7 (20.6)		

CI: confidence interval; TOP: termination of pregnancy; IUFD: in utero fetal death.

Table 3. Analysis of the accuracy of the postmortem ultrasound examination.

	Overall (n=123)	Gestational age < 20 weeks (n=37)	Gestational age ≥ 20 weeks (n=86)
All Organs			
Sensitivity (%)	74.7 (56/75) (64.8-84.5)	66.7 (12/18) (41.0-86.7)*	77.2 (44/57) (66.3-88.1)
Specificity (%)	83.3 (40/48) (70.0-92.5)*	73.7 (14/19) (48.8-90.9)*	89.7 (26/29) (72.7-97.8)*
Concordance rate (%)	78.0 (96/123) (70.7-85.4)	70.3 (26/37) (55.5-85.0)	81.4 (70/86) (73.2-89.6)
Discordance rate (%)	6.5 (8/123) (3.3-12.3)*	5.4 (2/37) (0.7-18.2)*	7.0 (6/86) (3.2-14.4)*
Non-diagnostic (%)	15.5 (19/123)	24.3 (9/37)	11.6 (10/86)
Brain (n=70 diagnostic at conventional autopsy)			
Sensitivity (%)	61.9 (13/21) (40.9-79.3)*	/ n=0	61.9 (13/21) (40.9-79.3)*
Specificity (%)	77.6 (38/49) (65.9-89.2)	83.3 (15/18) (58.6-96.4)*	74.2 (23/31) (55.4-88.1)*
Concordance rate (%)	72.9 (51/70) (62.4-83.3)	83.3 (15/18) (58.6-96.4)*	69.2 (36/52) (56.7-81.8)
Discordance rate (%)	8.6 (6/70) (4.0-17.5)*	0 (0/18)	11.5 (6/52) (5.4-23.0)*
Non-diagnostic (%)	18.6 (13/70)	16.7 (3/18)	19.2 (10/52)
Thorax excluding heart (n=123 diagnostic at conventional autopsy)			
Sensitivity (%)	26.3 (5/19) (9.2-51.2)*	0 (0/2)	29.5 (5/17) (10.3-56.0)*
Specificity (%)	80.8 (84/104) (73.2-88.3)	68.6 (24/35) (53.2-84.0)*	87.0 (60/69) (76.7-93.9)*
Concordance rate (%)	72.4 (89/123) (64.5-80.3)	64.9 (24/37) (49.5-80.3)	75.6 (65/86) (66.5-84.7)
Discordance rate (%)	10.6 (13/123) (5.1-16.0)	2.7 (1/37) (0.1-14.2)*	14.0 (12/86) (6.6-21.3)
Non-diagnostic (%)	17.1 (21/123)	32.4 (12/37)	10.5 (9/86)
Heart (n=122 diagnostic at conventional autopsy)			
Sensitivity (%)	50.0 (13/26) (30.8-69.2)	0 (0/6)	65.0 (13/20) (43.3-81.9)*
Specificity (%)	81.3 (78/96) (73.4-89.1)	77.4 (24/31) (58.9-90.4)*	83.1 (54/65) (74.0-92.2)
Concordance rate (%)	74.6 (91/122) (66.9-82.3)	64.9 (24/37) (49.5-80.3)	78.8 (67/85) (70.1-87.5)
Discordance rate (%)	5.7 (7/122) (2.8-11.4)*	8.1 (3/37) (1.7-21.9)*	4.7 (4/85) (1.9-11.5)*
Non-diagnostic (%)	19.7 (24/122)	27.0 (10/37)	16.5 (14/85)
Abdomen (n=123 diagnostic at conventional autopsy)			
Sensitivity (%)	60.7 (17/28) (42.6-78.8)	71.4 (5/7) (29.1-96.3)*	57.1 (12/21) (34.0-78.2)*
Specificity (%)	75.8 (72/95) (67.2-84.4)	73.3 (22/30) (54.1-87.7)*	76.9 (50/65) (66.7-87.2)
Concordance rate (%)	72.4 (89/123) (64.5-80.3)	73.0 (27/37) (58.7-87.3)	72.1 (62/86) (62.6-81.6)
Discordance rate (%)	12.2 (15/123) (6.4-18.0)	8.1 (3/37) (1.7-21.9)*	14.0 (12/86) (6.6-21.3)
Non-diagnostic (%)	15.4 (19/123)	18.9 (7/37)	14.0 (12/86)

* Exact confidence interval

Figure legends.

Figure 1. Study flowchart and diagnosis of each organ group with postmortem US and conventional autopsy. AN: abnormal examination findings, N: normal examination findings, ND: non-diagnostic examination. WG = Weeks gestation.

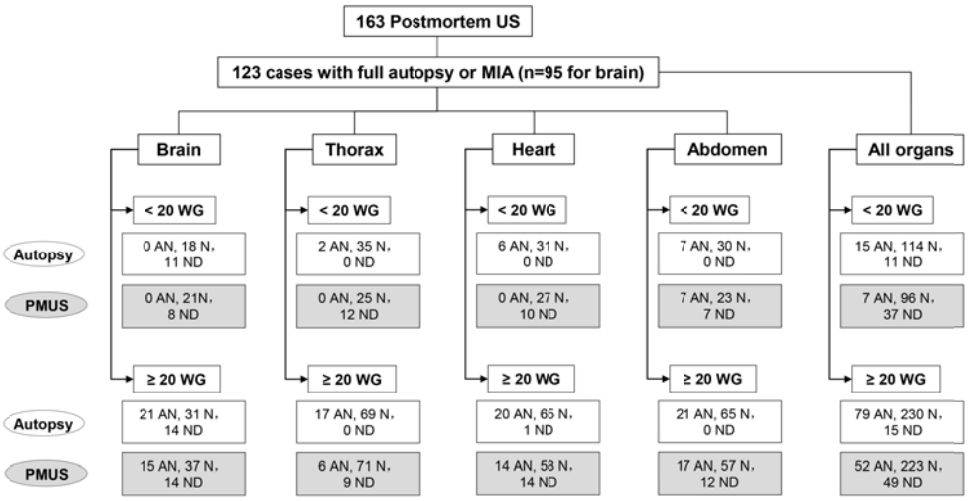

Figure 2. Postmortem ultrasound imaging.
14 week gestation fetus delivered following spontaneous premature rupture of the membranes. (A) Axial view of fetal brain showing the eyes (arrows), but the brain was non-diagnostic. (B) Axial view of fetal chest showing both lungs and the heart situs, but the details of the heart were not discernible.(C) Axial view of fetal abdomen showing the liver (Li) and the stomach (St). (D, E) Sagittal views of the fetal trunk showing the diaphragm (D) and the bladder (Bl) and spine. LL: left lung; RL: right lung.

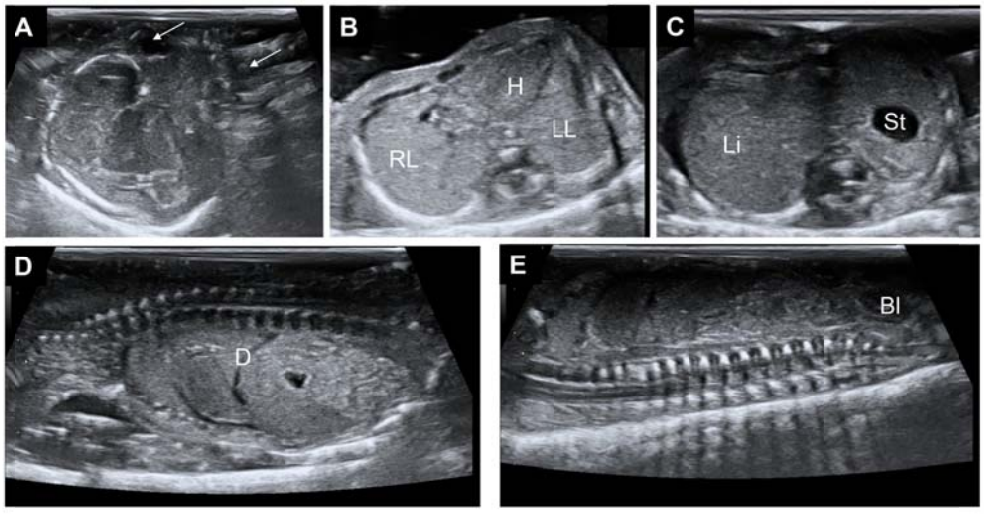

Figure 3. Postmortem fetal brain ultrasound examples.
25 weeks gestation fetus following termination of pregnancy due to agenesis of the corpus callosum. (A) Axial view of fetal brain showing absence of the cavum of the septum pellucidum (arrow) and (C) sagittal view showing agenesis of the corpus callosum (arrow), in comparison to images of a 28 week gestation fetus with normal septum pellucidum (arrow; B) and a normal corpus callosum (arrow; D).

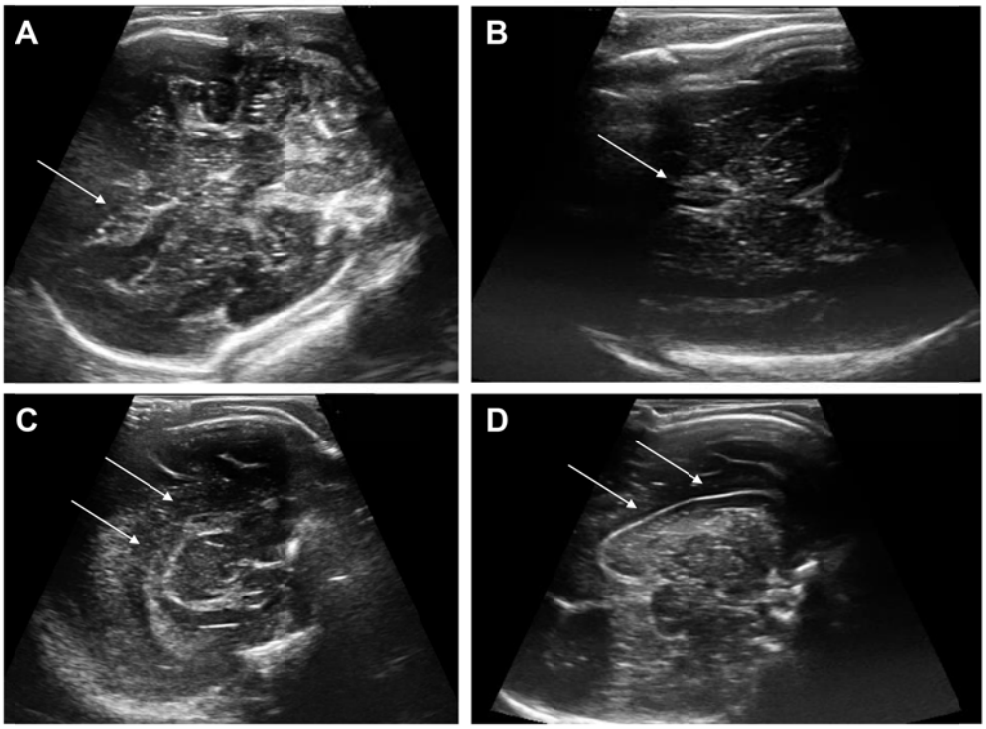

Figure 4. Postmortem fetal brain ultrasound examples.
(A) 29 weeks gestation fetus following termination of pregnancy due to congenital toxoplasmosis. Sagittal view of fetal brain showing an echogenic nodule (arrow head) compatible with calcification. Note the normal shape of the corpus callosum (arrows).
(B) Axial view of fetal brain at 34 weeks showing an echogenic nodule (arrow) compatible with a tuber in a fetus affected by tuberous sclerosis.
(C) Axial view of fetal brain at 20 weeks showing a severe hydrocephaly in a fetus affected by spina-bifida.
(D) Axial view of fetal brain at 20 weeks, non-diagnostic imaging secondary to severe maceration following unexplained in-utero fetal death.

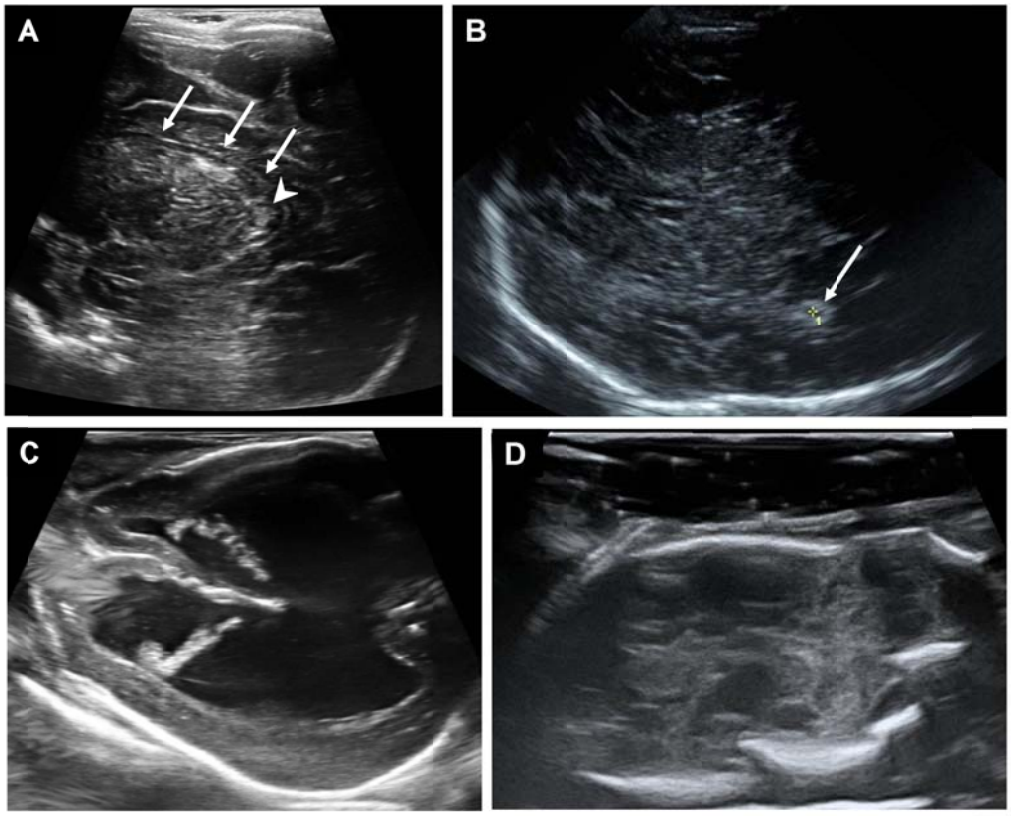

Figure 5. Postmortem fetal thoracic ultrasound.
29 weeks gestation fetus following termination of pregnancy due to brain anomaly.
(A) Axial view at the level of the chest showing a normal 4-chamber view (RV: right ventricle and LV: left ventricle) and (B) the emergence of the aorta (Ao) from the left ventricle.

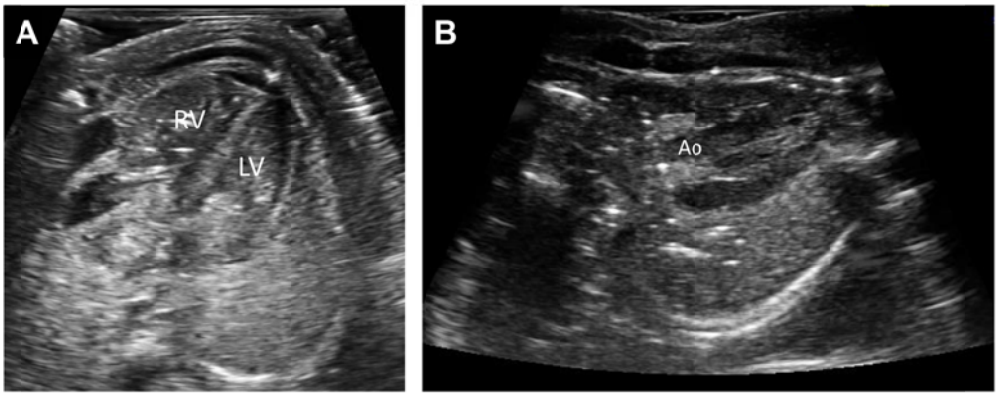

Figure 6. 34 weeks gestation fetus following termination of pregnancy due to tuberous sclerosis. (A) Axial prenatal ultrasound of fetal heart at the level of the left 4-chambers view showing hyperintens nodules compatible with rhabdomyomas. (B) Postmortem ultrasound with the corresponding image of the hyperintens nodule in the right and (C) in the left ventricle.

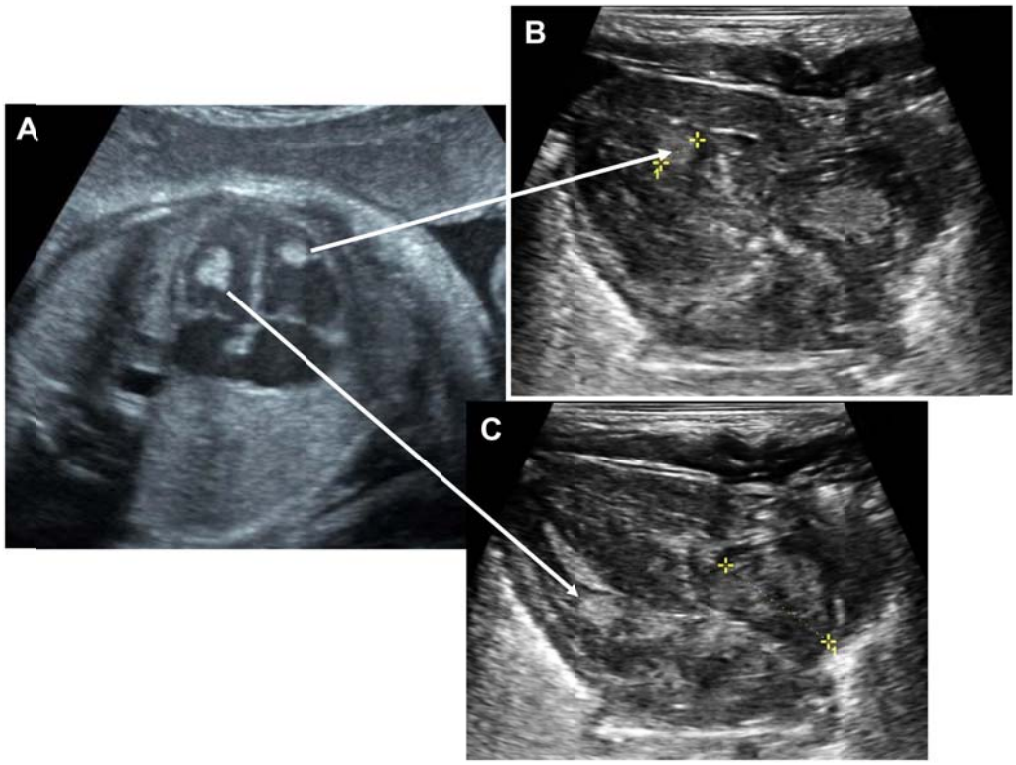

Figure 7. 28 weeks gestation fetus following termination of pregnancy due left-sided congenital diaphragmatic hernia. (A) Axial postmortem ultrasound of fetal thorax showing displaced abdominal organs into the left chest. (B) Axial postmortem ultrasound of fetal abdomen showing an intra-abdominal position of the liver. (C) Sagittal view of the same fetus showing herniation of the bowels, spleen, stomach and left kidney but not the liver. (D) Corresponding image with postmortem MR imaging.

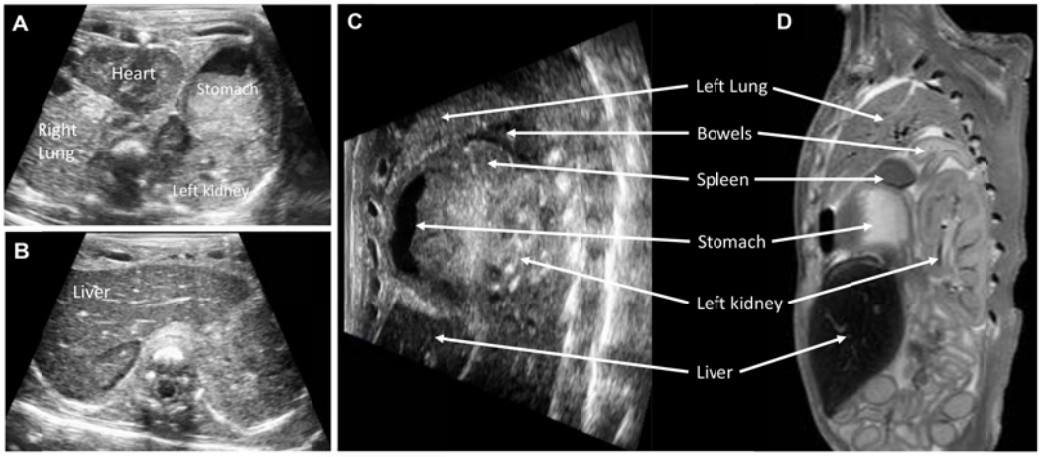

Figure 8. 29 weeks gestation fetus following termination of pregnancy due to polycystic kidneys with severe oligohydramnios. (A) Sagittal postmortem ultrasound of fetal abdomen at the level of the left kidney showing enlarged hyperechogenic kidney, above the 90th percentile for gestation measuring 41.1*23.2 mm, compatible with polycystic kidney. (B) Coronal postmortem MR imaging of the same patient with enlarged T2-WI hyperintens appearance of both kidneys. (C) 26 weeks gestation fetus with multi-cystic renal dysplasia. (D) Patient at 29 weeks of gestation with normal appearance kidney.