Feasibility and experience of the MinImAL procedure: Minimally Invasive perinatal and paediatric Autopsies with Laparoscopically assisted tissue sampling

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Short title: Laparoscopic autopsy

Abstract

Objectives

Less invasive autopsy techniques have good acceptability to parents, but the published sampling adequacy of needle biopsy studies is generally poor. Minimally Invasive Autopsy with Laparoscopic assisted sampling (MinImAL) has the potential to increase the diagnostic yield of less invasive autopsy by improving the quality and quantity of tissue samples obtained, whilst concomitantly permitting visualisation, extraction and examination of internal organs through a small incision. We present the findings of the MinImAL procedure in a cohort of 103 unselected perinatal and paediatric cases performed at a tertiary referral centre over five years.

Methods

Following a pre-procedure 1.5 T whole-body post-mortem MRI, MinImAL autopsy was performed. Data was collected prospectively and analysed retrospectively. Chi-square analysis was used to compare the 'unexplained' rate of intrauterine deaths within the cohort with a previously published cohort of intrauterine deaths.

Results

MinImAL autopsy was performed successfully in 97.8% (91/93) of cases. We found satisfactory rates of adequate histological sampling in most major organs; heart (100%, 91/91 cases), lung (100%, 91/91 cases), kidney (100%, 91/91 cases), liver (96.7%, 88/91 cases), spleen (94.5%, 86/91 cases), adrenal glands (89%, 81/91 cases), pancreas (82.4%, 75/91 cases) and thymus (56%, 51/91 cases). Procedure duration was similar to standard autopsy. There was no statistically significant increase in the 'unexplained' rate for stillbirths that received MinImAL autopsy when compared with a previously published cohort of >1,000 cases.

Conclusions

MinImAL provides good histological yield from major organs with minimal cosmetic damage and can be learned by an autopsy practitioner. MinImAL is an appropriate minimally invasive alternative for the investigation of perinatal and paediatric deaths where consent to full autopsy is withheld, and may have applications in both high and low-middle income settings.

Introduction

Post-mortem examination can provide families with a cause of death following fetal demise, or the death of a child or infant,[1] with information obtained from the autopsy contributing to the management of future pregnancies in up to 40% of cases.[2] Autopsy also provides tissue for research into congenital disease,[3] acts as a comprehensive audit of obstetric practice,[4] and offers a method of infectious disease surveillance in low or middle income countries.[5, 6] However, fewer than half of parents who experience a stillbirth provide consent, while for neonatal deaths, only around one quarter of parents agree to autopsy.[7] Contributing reasons include the invasive nature of the procedure, ambivalence regarding the value of autopsy, and religious objections.[8] In low-income countries, performance of autopsy is highly variable, both for aforementioned factors and lack of suitable infrastructure and availability of trained professionals,[9, 10] despite a strong interest in establishing a cause death within communities.[11]

Less Invasive Autopsy (LIA) approaches (Appendix 1) to both adult[12] and paediatric/perinatal autopsies[6, 13, 14] are a potential solution, with growing evidence to suggest that these investigations are acceptable to relatives of the deceased and health professionals.[15-17] Percutaneous needle organ sampling has been described in high-income countries, albeit with poor sampling performance thus far.[18-20] More recent data using percutaneous needle-core sampling[21] shows that MIA can provide a cause of death in up to 89% (100/112) of HIV infected adults[5] and up to 96% (52/54) of post-neonatal children,[6] however, sampling

adequacy was highly variable, which could limit applicability outside of the context of disseminated infectious disease.

One method to improve tissue yield is to utilise laparoscopically assisted "keyhole" examination, extraction and sampling of internal organs via a small incision. Parental acceptability of such a technique is high within the UK, even within religious communities, who view it as more acceptable than traditional autopsy.[8, 16, 17] Although proof of principle of such an approach has been reported,[13] the yield of such a technique in a larger cohort of cases remains undetermined.

This study presents the findings from 103 unselected cases that underwent Minimally Invasive Autopsy (MIA) with Laparoscopically assisted sampling (MinImAL procedure).

Methods

Study recruitment & consent

The study was approved by a national research ethics committee (REC 09/H0713/2) and all samples handled in accordance with the Human Tissue Act (2004). All parents provided informed written consent. One hundred and ninety perinatal / paediatric autopsies referred to our centre as part of routine clinical care were prospectively recruited to LIA between June 2011 and October 2016 (Figure 1), following the first ten cases previously reported in a feasibility study.[13] The cases were unselected, other than provision of parental consent for LIA or where specifically agreed between HM Coroner and the performing pathologist. Where examinations were consented procedures (rather than medico-legally required), parents were counselled regarding standard operating procedures of the role of and indications for standard autopsy, and offered standard autopsy initially, with LIA offered following refusal of standard autopsy. Parents could also restrict the MinImAL or standard autopsy to a specific body cavity or organ cavity, termed a "limited" autopsy, despite the lack of information regarding the added value of laparoscopic assisted sampling in this context. Some parents specified that a MinImAL could be performed initially, with

conversion to a standard autopsy if required. Parents who declined full or MinImAL autopsy were offered Non-Invasive Autopsy (NIA) involving postmortem magnetic resonance imaging (PMMRI), external examination and placental examination, with no tissue sampling.

MinImAL Procedure Protocol: Imaging

Pre-autopsy 1.5 T PMMRI was performed as previously described in all cases.[22] PMMRI results were reported by a specialist paediatric radiologist with expertise in post-mortem imaging (OJA, SCS) and discussed with the reporting pathologist (NJS or JCH) in light of the clinical information provided in the referral prior to the autopsy. Routine external examination of the body along with genetic and microbiological sampling was performed as usual for all cases. Placental examination was performed as part of the fetal autopsy, where available. The brain was only extracted when there was a clinical indication to do so, or if an abnormality was discovered on post mortem MRI,[23] with appropriate parental consent.

MinImAL Procedure Protocol: Visualisation, extraction & sampling.

The rationale and initial methodology for some aspects of laparoscopically assisted visualisation and sampling has been previously reported in a feasibility study. [13] In this study, a straight laparoscope (2, 4, or 10mm diameter according to body size) was passed into the abdominal cavity via a small epigastric incision (1-2cm, figure 2), and used to visualise the internal organs. Additional instruments (scalpel, forceps, scissors) were passed through the entry port to aid dissection for organ extraction and tissue sampling. Organ extraction, if deemed desirable by the operator and within parental consent, was performed as follows:

1. Incision of the rectum followed by blunt dissection of the intestines using Spencer-Wells forceps to the level of the duodenum.

2. Removal of the liver by freeing the diaphragmatic attachments using curved scissors, followed by piecemeal removal (usually achievable in two to three pieces in fetal cases).

3. En-bloc removal of the stomach, spleen, pancreas and duodenum by making a transverse incision is made at the level of the gastro-oesophageal junction and the posterior attachments are then dissected.

4. Removal of the adrenal glands and urinary tract by blunt dissection from the posterior abdominal wall under laparoscopic and direct vision.

5. En-bloc removal of the thoracic contents utilising an inferior approach. First, incision of the periphery of the diaphragm is performed, followed by dissection of the anterior attachments of the thymus and mediastinum and incision of the posterior attachments at the anterior aspect of the thoracic spine. The block is then freed by a blind, transverse incision of the trachea and oesophagus. The entire block can then be removed through the abdominal entry port.

Following external examination, the organs were sampled for histology and returned to the body through the entry point prior to reconstruction (Figure 3).

Initially, the first seven cases underwent MinImAL procedure followed by standard autopsy (with parental consent) of the abdomen and thorax by extending the MinImAL incision to a standard 'T' or 'Y' incision; however, in all cases, the major organs had been successfully laparoscopically eviscerated or sampled, and no further useful information was gained through the invasive procedure. Conversion to standard autopsy was subsequently only performed for specific indications or inadequate visualisation. An attempt to sample major organs (pre-defined as: heart, lung, kidney, liver, spleen, adrenal, pancreas and thymus) was made in all cases that were not limited by consent.

Following autopsy examination, all organs were returned to the body, which was released to the families following reconstruction. An autopsy report was then generated, containing the post-mortem radiology, histology, microbiology and genetic results, as per normal clinical practice.

Evaluating the MinImAL procedure: Sampling adequacy & timing

The primary outcome of this study was the rate of tissue sampling success following MinImAL procedure, which was pre-defined as sufficient material for the reporting pathologist to make a diagnosis of normal or abnormal. In each complete MinImAL case (n=93), an attempt was made to sample pre-defined major organs (heart, lung, liver, kidneys, adrenal glands, spleen, pancreas, thymus). Sampling failure was pre-defined as either insufficient material for comment, cases where the tissue sample was too small to survive histological processing or where the target organ was not sampled. Autopsy and

histological findings were compiled contemporaneously using the Great Ormond Street Hospital autopsy database and analysed retrospectively according to specific organ pathology/normality and analysis of sampling adequacy using Microsoft Access and Microsoft Excel (Microsoft, Seattle, USA).

The secondary outcomes were evaluation of MinImAL procedure duration in a subgroup of cases, cause of death analysis of the cohort, and comparison of the proportion of intrauterine fetal deaths (IUFDs) and stillbirths that remained unexplained following MinImAL procedure with that of a previously reported, unselected cohort of >1,000 IUFDs examined at the same centre during a similar time period.[24]

To evaluate whether the MinImAL procedure could be applied in day-to-day autopsy practice, a skilled operator familiar with standard autopsy but inexperienced with MinImAL (JCH) was trained over three familiarisation cases and subsequently timed for an unselected series of complete MinImAL procedures. The overall examination duration (the duration of organ inspection, evisceration (if deemed necessary by the operator), dissection and sampling) for was recorded. A Mann-Whitney U test (StatsDirect, Cambridge, UK) was performed to examine whether there was a statistical difference in procedure duration between the first and last ten cases timed (Appendix 2).

Although this study was not a formal diagnostic accuracy trial of the MinImAL procedure, a preliminary evaluation of the rate of 'unexplained' cases was necessary in order to establish whether use of the MinImAL procedure resulted in a statistically significant increase in the

number of 'unexplained' deaths as compared to standard autopsy. In order to do this, the 'unexplained' rate across the stillbirth and IUFD cases within the MinImAL cohort was compared to the published rate from a large case series of >1,000 IUFDs that underwent standard autopsy at the same centre[24] using Chi-Square analysis (StatsDirect, Cambridge, UK)(Appendix 3).

Results

Recruitment and demographics

Of 1,900 referrals to our institution for autopsy examination between June 2011 and October 2016, 190 cases underwent LIA, with the remainder undergoing standard autopsy. Of these 190 cases, 20 early gestation fetuses were specifically referred for micro-CT examination, the results of which have been published.[25] In 67 cases, the parents consented only for NIA involving PMMRI, external examination and placental examination, with no tissue sampling. The remaining 103 cases underwent MinImAL procedure with both PMMRI and laparoscopically-assisted organ examination and sampling. Of the 103 MinImAL cases presented in this study, 93 were fetal (age range: 15-41gw, median age: 23gw) including 59 terminations of pregnancy (all performed for fetal abnormalities), 28 IUFDs and six intrapartum stillbirths. The remaining ten cases included six neonatal deaths (age range: 21 minutes – 11 days, median age: 5 days), three infant deaths (age range: 3-4 months, median age: 3 months) (of which one was a sudden unexpected death in infancy (SUDI)) and one childhood death. Further demographic details are presented in table 1.

Consent and conversion rate

Of the 103 MinImAL cases, 99 were consented procedures, with another four undertaken on the authority of HM Coroner but at parental request. Ninety-three cases underwent complete MinImAL procedure, without restriction to a body system or cavity and of these 91 (97.8%) were successfully completed. In two cases (2.2%, 2/91), conversion to standard autopsy was required, one due to small fetal size (in a 16gw fetus with biometry of 14-15gw), the other due to poor visualisation in Prune-Belly Syndrome. The first seven cases of

this series underwent MinImAL with subsequent conversion to standard autopsy as part of technical optimisation. In 10 cases, a limited MinImAL procedure was performed, either by parental or Coronial request. In these cases, there was usually an organ-specific clinical question based on the clinical presentation.

Diagnostic performance of the MinImAL procedure: procedure duration

Examination duration was noted in a sub-series of 21 initial cases (Figure 4). This series demonstrated a considerable learning effect, with a Mann-Whitney U test showing a significant difference between the median procedure duration of the first ten (26 minutes, 30 seconds) and last ten procedures (18 minutes) (Appendix 2), $p<0.0001$.

Diagnostic performance of the MinImAL procedure: sampling adequacy

Heart, lung and kidney were successfully sampled in every case (100%, 91/91). Liver was successfully sampled in 96.7% (88/91), spleen in94.5% (86/91) and adrenal gland, pancreas and thymus in 89.0% (81/91), 82.4% (75/91) and 56.0% (51/91) of cases respectively (Table 2).

Diagnostic performance of the MinImAL procedure: contribution of histology

Of the 91 cases in the cohort that underwent successful complete MinImAL examination, significant histological abnormalities (excluding CNS) that contributed to the cause of death were demonstrated in 16 organs from nine individual cases (Table 3). Significant abnormalities were identified within the heart (2/91, 2.2%), lungs (3/91, 3.3%), kidneys

(7/91, 7.7%), liver (3/91, 3.3%) and spleen (1/91, 1.1%, figure 5). Of the organs with a histological abnormality present, in all but two (both involving the heart), a clinical, radiological or macroscopic abnormality was present. Both of the cases with unsuspected cardiac abnormalities were post-natal deaths (one at day 11, one at four months). In no case of fetal death did histological sampling without a clinical, radiological or macroscopic indication to sample the organ reveal additional information that contributed to the cause of death.

Diagnostic performance of the MinImAL procedure: Overall cause of death

The unexplained rate across the cohort (defined as a non-diagnostic autopsy in Termination of Pregnancy (ToP) cases) was 47% (16/34 cases) in IUFD and stillbirth cases, 25% (1/4 cases) in infant / childhood deaths, 17% (1/6 cases) in neonatal cases and 5% (3/59 cases) in ToP cases. Placental causes of death were identified in 41% (14/34 cases) of IUFD / stillbirth cases. The presence of genetic disorders and congenital anomalies also contributed significantly to death within the cohort, with 50% (5/10) of neonatal, infant and childhood deaths involving a clinical history of a genetic disorder and 90% (53/59) of ToP cases performed for either a congenital anomaly or genetic disorder that was confirmed at MinImAL examination. A summary of the overall causes of death obtained across the cohort is shown in Figure 6, with a further breakdown of the IUFD and stillbirth cases in

Figure 7, and specific yield charts by for components of MinImAL according to age group in appendix 4.

Diagnostic performance of the MinImAL procedure: unexplained rate

Whilst this study was not designed as a trial to evaluate the accuracy of the MinImAL procedure, Chi-Square analysis revealed no significant difference in the 'unexplained' rate between this cohort and over 1,000 IUFDs previously published [24] (Appendix 3), p=0.0945.

Discussion

This study presents our initial experience with a large, unselected cohort of perinatal and paediatric autopsies performed using the MinImAL procedure, along with analysis of sampling adequacy and histological abnormalities. We have demonstrated that such approaches can be learnt and performed in a reasonable time frame, with a low failure rate (2.2%, 2/93). Our findings suggest that the MinImAL procedure has a similar performance to standard autopsy in terms of the proportion of IUFD / stillbirth cases in which a cause of death is determined. Given that recent data indicate that LIA techniques have a high degree of acceptability for parents and religious communities,[8, 16, 17] these findings have implications for perinatal autopsy practice globally, as the acceptability of the standard autopsy continues to decline.

Our study had a low rate of MinImAL cases requiring conversion to standard autopsy due to technical difficulty or poor visualisation and good sampling adequacy compared with published studies (Table 4). Potential reasons for sampling failure include operator error (e.g. failure to sample the organ), identification error (e.g. sampling fat instead of adrenal gland), failure to locate the target organ, and failure of a sample to survive histological processing. This is illustrated by three early gestation cases in which sampling of the liver failed due to advanced maceration, as an adequate amount of sample for histological interpretation did not survive tissue processing.

There was no significant difference in the unexplained rate between the MinImAL cohort and a previously published cohort of >1,000 IUFD cases from the same centre, suggesting that overall performance is likely to be similar to standard autopsy in this population. Examination of the placenta is clearly important within the IUFD / stillbirth sub-group as it accounted for 41% (14/34) of these deaths. In this study, non-neurological visceral histology provided a significant contribution to the cause of death in nine cases. In only two cases (both postnatal deaths, both involving the heart) did histology of a macroscopically, clinically and radiologically normal organ provide the cause of death. In all other cases within the cohort, histological abnormalities were discovered within the context of clinical, radiological or morphological indications to sample the organ. A previous study examining the contribution of routine histology in the context of IUFD found that only around 1% of cases demonstrated histological abnormalities which provided the cause of death when the internal organs appears normal macroscopically,[26] which is in keeping with our findings.

The rationale for the development of the MinImAL procedure derives from multiple studies demonstrating that needle biopsy of organs within the post-mortem setting yields high rates of 'inadequate' tissue samples,[18-20] thus potentially hindering investigation after death. We have demonstrated that the MinImAL procedure can be learned by an autopsy practitioner, and applied within clinical practice, with good sampling rates of most organs, and a reasonable performance duration. The MinImAL approach therefore provides a potential solution to the problem of sampling adequacy for tissue-based investigations. Although the time required for examination of the thoracic and abdominal cavities may be prolonged using the MinImAL procedure, the use of pre-autopsy PMMRI in this study meant that in many cases, further extraction and examination of the brain was not necessary, balancing this out. Moreover, PMMRI has been reported to increase diagnostic accuracy in cases with marked maceration[23] and as such can provide the reporting pathologist with a useful additional source of information. The equipment used for the laparoscope-assisted portion of this study (Karl-Storz Tele Pack X LED) is a relatively low cost, portable option, providing visualisation in fetuses as small as 15 gw. Laparoscopy data can be saved directly to a USB flash drive, avoiding the need for expensive data storage systems. Although an incision is required through which to insert the laparoscope, this is much smaller than a standard autopsy incision, and could theoretically reduce the risk to the operator from aerosolisation of pathogens (insufflation is not required for a MinImAL procedure). From a consent perspective, many parents already have a preconception about incisional approaches from the use of laparoscopic compared to open surgical approaches in the adult surgical setting.[8]

The MinImAL approach could therefore potentially be applied within low and middle-income settings, following suitable training of local operators. This has significant implications for investigations after death in high income countries, where acceptability of standard autopsy remains low, and low or middle-income countries, where community acceptance of autopsy and resources can be patchy, even in major cities.

Although we attempted to study an unselected cohort of cases, parents were required to specifically consent to minimally invasive autopsy. It is possible that this contributed to the relatively high proportion of ToP cases within the cohort, although our methodology was largely the same across all cases, as is true for standard autopsy. We acknowledge that it is not currently possible to extract the brain for a detailed neuropathological examination or an entire long bone using the MinImAL approach. Suspicion of pathology in these areas may therefore necessitate an additional incision.

It is difficult to compare the findings of the MinImAL procedure to a reference standard (i.e. standard autopsy), as following a complete MinImAL procedure, few internal organs remain within the body cavity following conversion to full autopsy. Due to the rarity of some of the conditions encountered in clinical practice, a full diagnostic accuracy study of the MinImAL procedure would potentially require thousands of cases to be compared with a historical cohort of standard autopsy cases.

Economic cost-benefit analysis addressing, for example, the cost of training pathologists and a potential increase in case numbers with improved acceptability should also be performed.

With adequate training, the MinImAL approach could also potentially be applied to low and middle-income settings, where community acceptance of autopsy and resources are limited, although organisational implications for introduction of such a service remain undetermined. Finally, optimisation of algorithms for selection of cases most appropriate for MinImAL across a wide range of clinical scenarios is required.

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Conflicts of interest

The authors declare they have no competing interests.

Role of Funding Source

The funder of the study had no role in the study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author and chief investigator (JCH, NJS) had full access to all the data in the study and final responsibility for decision to submit for publication.

Ethical approval and consent to participate

The study was approved by a national research ethics committee (REC 09/H0713/2) and all samples handled in accordance with the Human Tissue Act (2004). Written consent was obtained in each case.

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Figure legends

Figure 1. Flowchart of study recruitment. MIA = minimally invasive autopsy, Micro-CT = microcomputed tomography, NIA = non-invasive autopsy, PMMRI = post-mortem MRI

Figure 2. Demonstration of the incision size (approximately 1-2cm) required for the MinImAL procedure in a macerated term stillbirth (A), alongside a photo following reconstruction of the body (B). This incision permitted inspection, removal, macroscopic examination (as per a standard autopsy) and replacement of all of the thoracic and abdominal viscera.

Figure 3. Heart and lung block extracted intact following MinImAL procedure, prior to macroscopic dissection and examination. Even in small fetuses, organs can be extracted with relative ease using this technique.

Figure 4. Time taken to perform MinImAL procedure by a single operator over 21 cases, with trend line.

Figure 5. Illustration of a 24gw fetus with hepatosplenomegaly seen on T2-weighted PMMRI (coronal section of the thorax and abdomen) (A), with spleen histology obtained via laparoscopic sampling as part of a MinImAL procedure (B) [Haematoxylin and Eosin] & (C) [Diastase-PAS]). Numerous storage cells filled with DPAS positive material are present (arrowheads).

Figure 6. Causes of death within the cohort as percentages of the total number of terminations of pregnancy (ToP, n = 59), intrauterine fetal deaths and stillbirths (IUFD / stillbirth, n = 34), neonatal deaths (Neonatal, n = 6) and infant and childhood deaths (n = 4).

Figure 7. Analysis showing the causes of death within the intrauterine fetal death and stillbirth groups from the cohort.

Table 1

Type of MinImAL (n = 103)	Coronial	4
	Consented	99
Indication	Termination of pregnancy	59
	Intrapartum stillbirth	6
	IUFD	28
	Neonatal death	6
	Infant (of which, SUDI)	3 (1)
	Child/Adolescent	1
Gestational age of fetal cases (n = 93)	Mean	25.5 gw
	Median	23 gw
	Range	15-41 gw

Table 1. Demographics of the 103 cases accepted for any form of MinImAL examination.

IUFD = intrauterine fetal death, gw = gestational weeks, SUDI = sudden unexpected death in infancy

Table 2

	Heart	Lung	Kidney	Liver	Adrenal gland	Pancreas	Spleen	Thymus
Sampled successfully, histology normal or non-contributory to death	89 (97.8%)	88 (96.7%)	84 (92.3%)	85 (93.4%)	81 (89.0%)	75 (82.4%)	85 (93.4%)	51 (56.0%)
Sampled successfully, histology abnormal and contributed to death	2 (2.2%)	3 (3.3%)	7 (7.7%)	3 (3.3%)	0	0	1 (1.1%)	0
Total sampling success	91 (100%)	91 (100%)	91 (100%)	88 (96.7%)	81 (89.0%)	75 (82.4%)	86 (94.5%)	51 (56.0%)
Sampling failure	0	0	0	3 (3.3%)	10 (11.0%)	16 (17.6%)	5 (5.5%)	40 (44.0%)

Table 2. Histological sampling success rates and normality/abnormality rates across major organs in the 91 complete, unconverted MinImAL cases.

Table 3

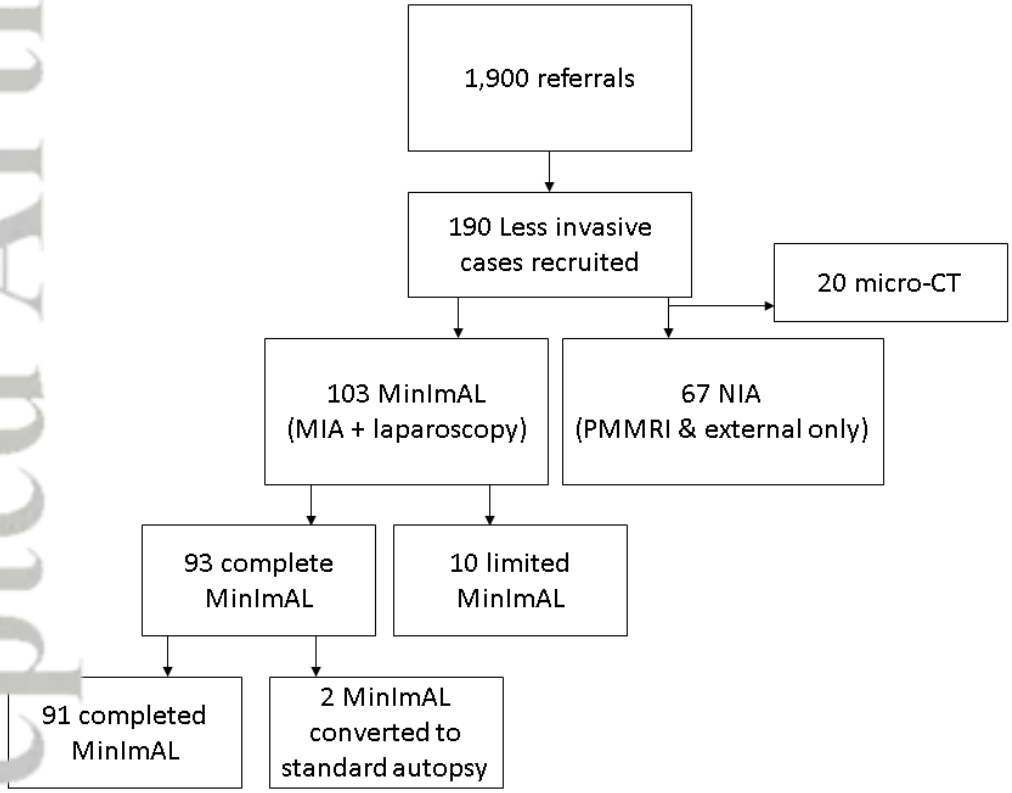
	Heart	Lung	Kidney	Liver	Spleen
Histology abnormal & contributed to death	2	3	7	3	1
Macroscopic indication to sample organ	0	2	7	2	1
Radiological indication to sample organ	0	2	7	2	1
Clinical indication to sample organ	0	1	7	2	1
Organ clinically, morphologically and radiologically normal	2	0	0	0	0
Abnormalities on histology	2x infarction	1x ALI 1x DAD 1x pulmonary hypoplasia	3x dysplastic kidney 2x cystic dysplasia 1xATN 1x ARPKD	1x ductal plate malformation 1x fibrosis 1x cirrhotic fibrosis and necrosis	1x storage disorder

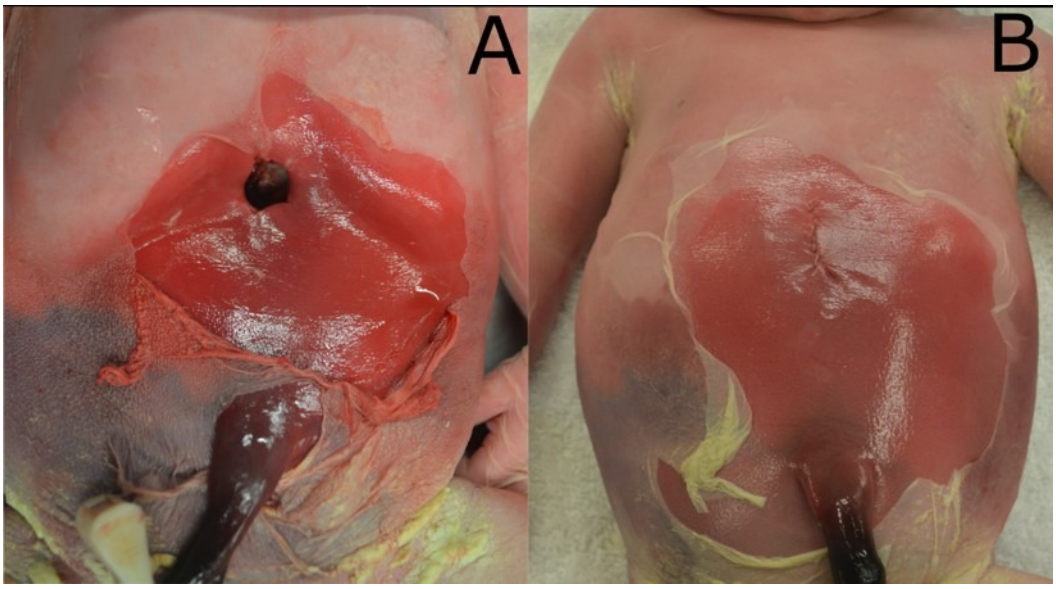
Table 3. Evaluation of the significant abnormalities found on non-neurological histological examination within the cohort of complete MinImAL cases, and the presence of clinically, radiologically or macroscopically suspected abnormalities in these cases. Sixteen organs from nine complete MinImAL cases showed significant abnormalities that contributed to death. ALI = acute lung injury, ARPKD = autosomal recessive polycystic kidney disease, ATN = acute tubular necrosis, DAD = diffuse alveolar damage,

				Adequacy rate of histological sampling by organ							
Study	n	Age range	Method	Heart	Lung	Liver	Kidney	Adrenal	Spleen	Pancreas	Thymus
This study	103 (91 for sampling analysis)	15 gw – 14 years	MinImAL (Laparoscopic, prior 1.5T MRI)	<u>100%</u>	<u>100%</u>	97%	<u>100%</u>	<u>89%</u>	<u>93%</u>	<u>82%</u>	<u>56%</u>
Garg[19]	25	33 gw – 28 days	Needle biopsy (blind percutaneous)	-	84%	92%	56% L 24% R	-	20%	-	-
Bansal[20]	50	12 – 80 years	Needle biopsy (blind percutaneous)	28%	90%	82%	48%	-	22%	18%	-
Breeze[18]	29	16 – 39 gw	Needle biopsy (USS guided, percutaneous)	52%	86%	76%	34%	41%	17%	-	17%
Bassat[6]	54	1 month – 15 years	Needle biopsy (percutaneous, prior USS)	47%	98%	<u>100%</u>	56%	32%	31%	8%	-
Castillo[21]	30	17 – 76 years	Needle biopsy (percutaneous, prior USS)	80%	100%	<u>100%</u>	67%	-	70%	-	-

Table 4.

Table 4. MinImAL histological sampling performance compared to other published studies, along with methodology used and cohort type. The best performing figures compared with other studies are underlined. gw = gestational weeks, MRI = magnetic resonance imaging, USS = ultrasound scan





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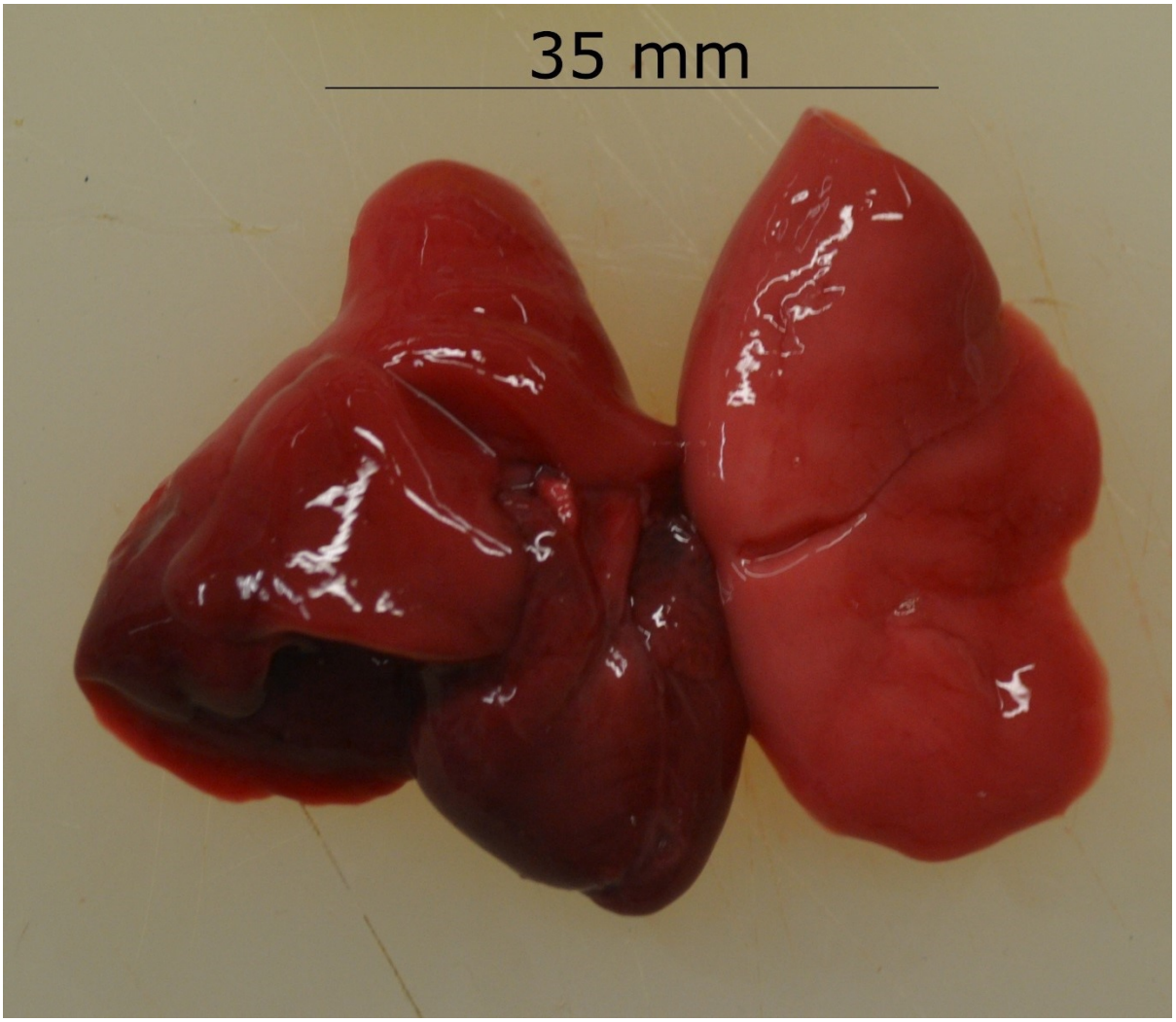

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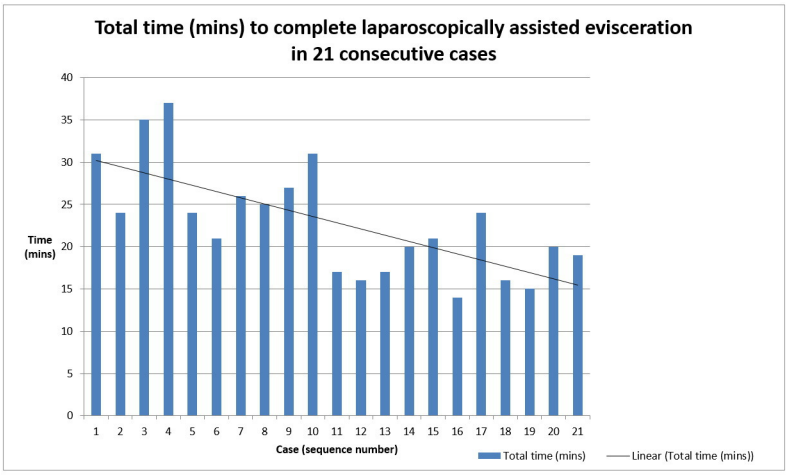

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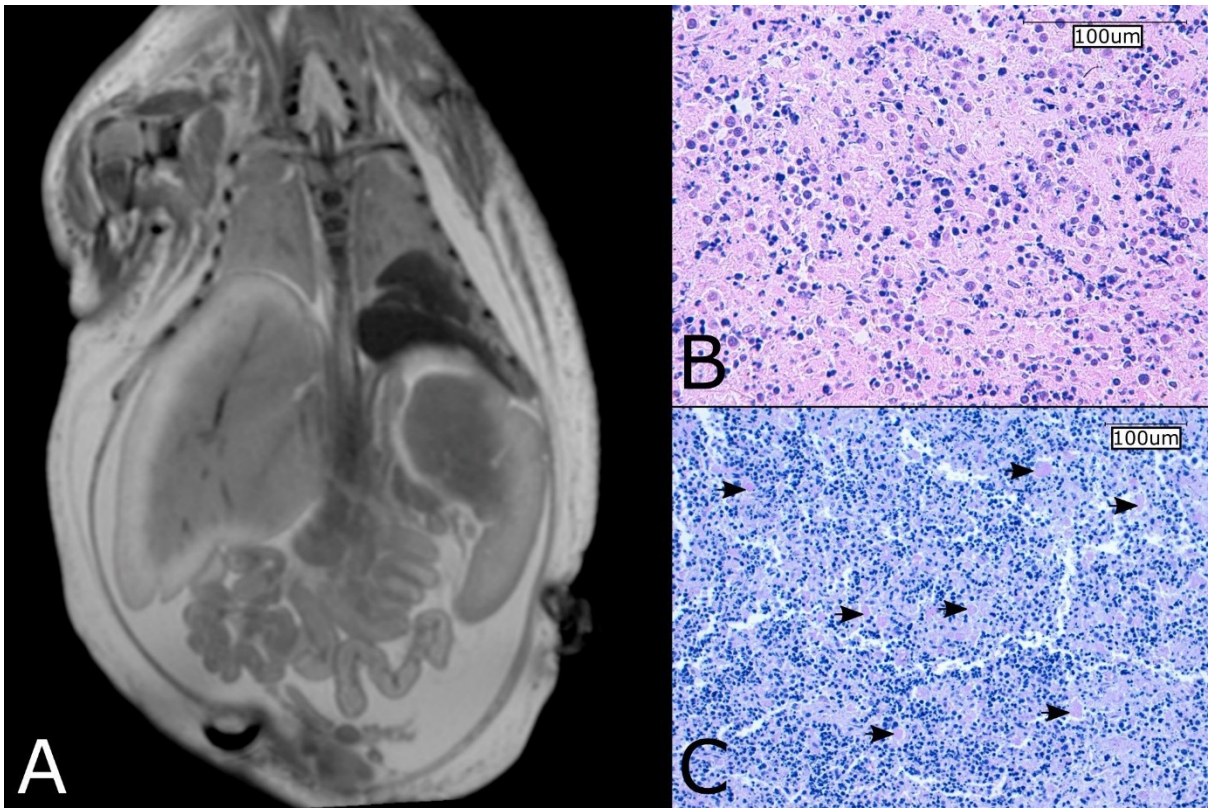

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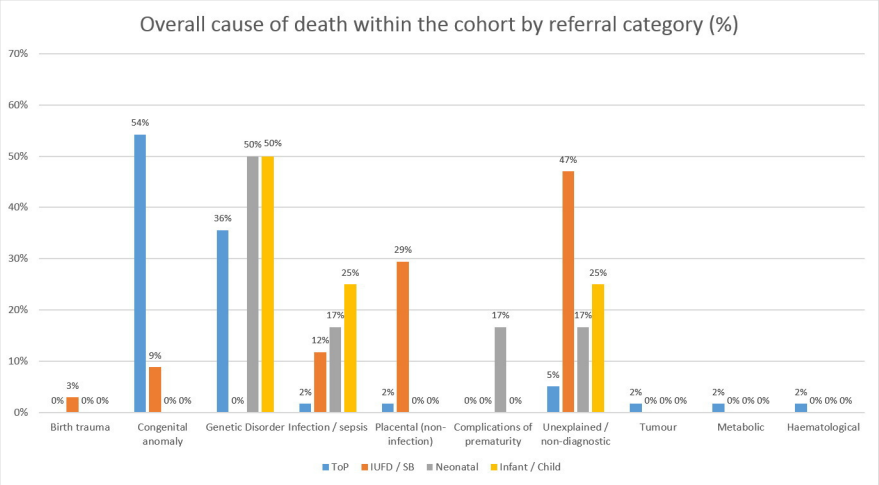

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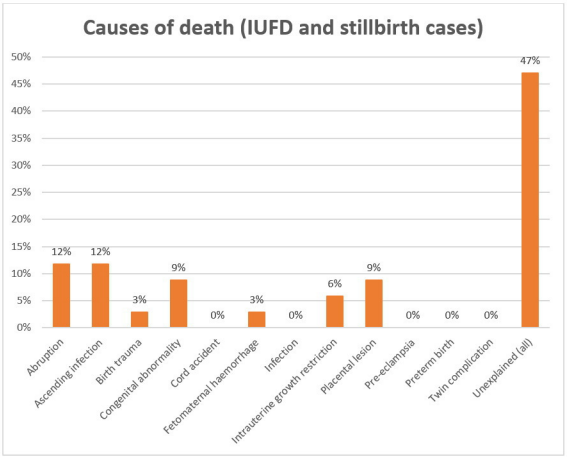

UOG_20211_Figure 7.jpg