Minimally invasive autopsy for fetuses and children based on a combination of post-mortem MRI and endoscopic examination: a feasibility study

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Declared competing interests of authors: none

Disclaimer: This report contains transcripts of interviews conducted in the course of the research and contains language that may offend some readers.

Published August 2019
DOI: 10.3310/hta23460

Scientific summary

Feasibility study of minimally invasive autopsy for fetuses and children

Health Technology Assessment 2019; Vol. 23: No. 46
DOI: 10.3310/hta23460

NIHR Journals Library www.journalslibrary.nihr.ac.uk

Scientific summary

Background

Consent rates for prenatal, perinatal and paediatric autopsy have dropped significantly in the UK in the past 30 years, despite evidence that autopsy can provide clinically significant findings in 22–76% of cases. National data show that less than half of parents of stillborn babies and only one-quarter of parents of neonates who died in 2014 provided consent for standard autopsy examination. In order to address these concerns and improve uptake rates, the feasibility of less invasive autopsy (LIA) techniques has been developed and evaluated in recent years. One promising approach is the use of cross-sectional imaging techniques, in particular magnetic resonance imaging (MRI). A large prospective trial reported that MRI-based imaging techniques along with other ancillary investigations, such as placental examination, genetic and metabolic tests [non-invasive autopsy (NIA)], had around 95% concordance for major diagnoses with conventional autopsy for fetuses. However, they were less accurate for newborns and children (85% and 54%, respectively), as imaging alone is unable to detect cases of systemic disease with no anatomical features, such as sepsis. MRI combined with targeted laparoscopic examination and biopsy of visceral organs [minimally invasive autopsy (MIA)] may be an alternative, as it combines the advantages of both imaging and tissue sampling, and it has been estimated that > 90% of significant histology findings from standard perinatal autopsies could be detected using a minimally invasive approach, although further evaluation is required.

Aims

The aims of this programme of research were as follows.

Empirical research with key stakeholders

The key research questions to address were:

- Is MIA and/or NIA more acceptable to parents than standard autopsy methods?
- How can alternative methods of investigating death fit into existing care pathways?
- Which patient populations are these methods most appropriate for?
- What is the best way to offer such a service to groups for whom standard autopsy is never acceptable (including specific ethnic and religious populations)?

To address these research questions we conducted three substudies.

Substudy 1

This was a mixed-methods study with bereaved parents who had experienced miscarriage, termination of pregnancy for fetal anomaly, stillbirth (SB), neonatal death or child death. The aim of this study was to determinate acceptability and likely uptake of LIA.

Substudy 2

This was an interview study with health professionals (who would either discuss autopsy with parents or conduct autopsy) and Her Majesty's (HM) Coroners. The aim of this study was to explore views towards LIA, including perceived benefits and concerns, and to identify how LIA should fit into existing care pathways.

Substudy 3

This was an interview study with religious leaders and focus groups with members of the Muslim and Jewish communities, who traditionally decline autopsy as it is not permitted by religious law, except in certain circumstances. The aim of this study was to determine if NIA and/or MIA was an acceptable alternative and under which circumstances.

Retrospective analysis of existing autopsy data

Analysis of existing autopsy data sources, including national data, retrospective autopsy series and existing LIA and MIA series, to provide estimates of the potential efficacy of MIA and its projected utility in clinical practice.

Methods

Systematic review of the literature

Prior to conducting empirical research, a systematic review was conducted in order to synthesise the current knowledge on bereaved parents' motivations for accepting or declining autopsy and to identify any knowledge gaps that called for more research. The evidence generated was used to inform the survey and interview questions with key stakeholders, as well as to provide background and context to the study topic.

Empirical research with key stakeholders

Parents and parent advocates were involved in the study from the outset. This included input into the survey design in terms of the questions and wording, revising the participants' information sheets and interview questions, and discussing and interpreting the key findings from the research to develop practical recommendations for practice.

Substudy 1: mixed-methods study with bereaved parents to determine acceptability and likely uptake of less invasive autopsy

This substudy comprised (1) a cross-sectional survey and free-text comments with bereaved parents; and (2) semistructured qualitative telephone interviews with a subset of survey responders. The main aim of the survey was to elicit participants' attitudes, likely uptake and preferences for NIA, MIA and conventional autopsy. Recruitment into the survey was conducted both retrospectively and prospectively. Bereaved parents were recruited retrospectively through the support groups Antenatal Results and Choices, Stillbirth and Neonatal Death Society, The Lullaby Trust, and Child Bereavement UK. Anyone who had experienced the loss of a pregnancy (through miscarriage, termination of pregnancy for a fetal abnormality or SB) or had experienced a neonatal or infant death was eligible to take part, irrespective of whether they had been offered an autopsy or an autopsy had been requested by HM Coroner's Office. Bereaved parents were also prospectively recruited through the fetal medicine units, delivery units or neonatal intensive care units of seven hospitals across England. Semistructured telephone interviews were conducted with a subset of survey responders. The topic guide explored participants' experience of being approached about standard autopsy (for those whom a coronial autopsy was not required), including reasons for accepting or declining and their views towards LIA (i.e. perceived advantages and potential concerns or limitations).

Substudy 2: interview study with health professionals and Her Majesty's Coroners

This was a qualitative study using semistructured interviews. Health professionals in the UK from a range of clinical backgrounds, who would be involved in discussions with parents about autopsy examination or who would conduct or interpret autopsy results, were purposively sampled. HM Coroners who are responsible for requesting autopsies in cases of unnatural or sudden deaths, including those in infancy and childhood, were also included. Interviews covered the following topic areas: views regarding full autopsy; factors affecting uptake and experience of consenting parents; views concerning LIA, including perceived benefits and potential limitations or concerns; views regarding implementation of LIA into clinical or coronial practice.

Substudy 3: interview and focus group study with religious leaders and community members

This was a qualitative study incorporating (1) interviews with religious leaders and community leaders; (2) focus groups with members of the Muslim and Jewish communities; and (3) interviews with Muslim or Jewish participants from substudy 1. Separate but related topic guides were developed for interviews and focus groups. The following topic areas were included: acceptability of traditional autopsy from a Muslim/Jewish perspective; personal views regarding LIA; permissibility of LIA from a Muslim/Jewish

perspective (both religious belief and practice); and likely uptake of NIA and MIA, both personally and within the community more generally. A Muslim chaplain and an Orthodox rabbi based in London, with links to a participating hospital, were identified as key informants who helped identify other religious and community leaders to invite into the study. Focus groups with members of two Muslim communities were arranged through representatives from the East Midlands Centre for Black and Minority Ethnic Health in Leicester and a Muslim community centre in Tower Hamlets, East London. For the Jewish community, these were arranged through a rabbi from the Orthodox community and a community leader with close links to the Haredi community, both in London, which has the UK's largest Jewish community.

Data analysis

For the quantitative survey data, frequencies were used to summarise the findings around autopsy acceptability, likely uptake and preferences. Chi-squared tests and independent samples *t*-tests were used to determine significant differences between groups. For the qualitative data, free-text comments, interviews and focus groups were analysed as one data set, using thematic analysis.

Retrospective analysis of existing autopsy data

Detailed data from autopsies conducted at Great Ormond Street Hospital since 1995 have been recorded in a dedicated autopsy database with > 400 variables/fields, with associated objective criteria described in a database handbook. For the purposes of this study, each case was classified as SB/intrauterine fetal death (IUFD), termination of pregnancy for fetal abnormality (ToP), sudden unexpected death in infancy (SUDI) or sudden unexpected death in childhood (SUDC), according to clinical presentation. For each case, all organs examined were recorded as being (1) normal, (2) abnormal but not relevant to cause of death or main diagnosis, (3) abnormal and possibly relevant to cause of death or main diagnosis, or (4) abnormal and definitely relevant to cause of death or main diagnosis, based on both macroscopic appearance and histological (microscopic) examination.

As part of data entry, judgements made by the reporting pathologist regarding the abnormalities present at internal examination and on histological examination were recorded according to predefined categories. These categories were independent of each other, so they could be used in any combination for macroscopic and microscopic examination, and could be explored further within free-text boxes in the database. These categories were also applied to placental examination and placental histology, when appropriate.

Following completion of data entry, data were extracted for all completed cases between 2005 and 2016, according to referral category (SUDI, SUDC, IUFD or ToP), and they were analysed using descriptive statistics, chi-squared tests and comparison of proportions tests when appropriate.

Results

Systematic review

Seven major themes describing barriers to autopsy uptake were identified: dislike of invasiveness; practicalities of the procedure; organ retention issues; protective parenting; communication and understanding; religion and culture and professional or organisational barriers. Six major themes related to factors which facilitated parental consent were identified: (1) desire for information, (2) contributing to research, (3) coping and well-being, (4) respectful care, (5) minimally invasive options and (6) policy and practice. There was a number of themes in the literature that reflected best practice.

Empirical research with key stakeholders

Substudy 1

Overall, 859 surveys were included in the analysis (68 prospective and 791 retrospective). A total of 90.5% participants indicated that they would consent to some form of LIA (MIA, NIA or both). A total of 53.8% participants would consent to standard autopsy, 74.3% to MIA and 77.3% to NIA. When dichotomising

experience into participants who had experienced fetal loss with participants who had experienced neonatal or child death, participants who had experienced neonatal and/or paediatric death were significantly more likely to think that MIA was acceptable and would be more likely to consent to it than those who had experienced fetal loss ($p < 0.05$ for both). Regarding parental preferences, 45.5% ($n = 391$) preferred MIA, 30.8% ($n = 265$) preferred NIA and 14.3% ($n = 123$) preferred standard autopsy, highlighting the need for provision of choice. Qualitative findings suggest that parents value NIA because of the lack of any incision and that MIA is considered a good compromise as it enables tissue sampling while easing the parental burden associated with consenting to standard autopsy.

Substudy 2

Twenty-five health professionals and four coroners participated. Participants viewed less invasive methods as a positive development that could potentially increase uptake. Practical-, psychological- and faith-related benefits included acceptability to parents and faith groups who object to invasive approaches; potential for faster turnaround times; parental familiarity with imaging and laparoscopic approaches; and those circumstances in which cross-sectional imaging might provide greater diagnostic accuracy. Concerns around the limitations of the technology, such as the unsuitability of imaging in certain circumstances, the potential for misdiagnosis and de-skilling the workforce, were identified. Implementation issues included access to scanning equipment, need for a multidisciplinary approach, training requirements, cost implications, equity of access and acceptance from health professionals.

Substudy 3

Muslim and Jewish religious- and faith-based authorities agreed that NIA with imaging was religiously permissible because it did not require incisions or interference with the body. A minimally invasive approach was less acceptable as it still required incisions to the body, although in circumstances in which it was required by law, it was considered more acceptable than a full autopsy. During focus group discussions with community members, the majority of participants indicated that they would potentially consent to NIA if the body could be returned for burial within 24 hours, or if a family had experienced multiple fetal/pregnancy losses and the information gained might be useful in future pregnancies. MIA was less acceptable; however, around half of participants might consent if NIA was not suitable, with the exception of the Jewish Haredi community who unanimously stated that they would decline this alternative.

Retrospective analysis

Data demonstrated that in 5–10% of SUDC and SUDI cases, the final cause of death is determined by routine histological sampling of macroscopically normal organs, predominantly the heart and lungs, with a few cases contributed by brain, liver and kidney examination. Routine histological sampling therefore remains an important aspect of investigation, even if post-mortem imaging appears normal. In contrast, routine sampling of any macroscopically normal organs only very rarely (< 0.5%) provided the cause of death in fetal cases (including SB/IUFD/ToP). The > 1% of cases in the SB/IUFD group represented detection of ascending infection on lung sampling, which would have been detected on placental examination and sampling, had this been available. Therefore, in fetal cases in which macroscopic examination for structural abnormalities/post-mortem imaging is normal there is little indication or yield from invasive organ sampling and histological examination to determine the cause of death or the main diagnosis. Targeted sampling of abnormal organs and lungs may be sufficient to identify abnormal and contributory cases.

Routine histological sampling of macroscopically normal organs in SUDI and SUDC cases is therefore recommended, whereas histological sampling of normal organs in fetal cases (including ToP, SB and IUFD) provides minimal useful information, and such cases are therefore potentially highly appropriate for LIA methods of investigation after death.

Implications for practice

Overall, participants viewed less invasive methods of autopsy as a positive development in perinatal and paediatric care, which could increase autopsy rates. However, several requirements must be put in place to make LIA a viable alternative for parents, including training of radiologists to interpret imaging results and pathologists to conduct image-guided biopsies, availability of scanning equipment, training for health professionals to offer LIA appropriately, and adapted consent procedures and consent forms.

Conclusion

Less invasive methods of autopsy are acceptable alternatives for bereaved parents, including those from the Muslim and Jewish faiths, and, if offered, are likely to increase uptake and improve parental experience. The data have demonstrated that, although extensive tissue and organ sampling is currently recommended, in the vast majority of cases such sampling does not significantly contribute to determination of the cause of death or the major diagnosis. Therefore, a more limited and targeted tissue sampling protocol could be introduced without significant reduction in accuracy of final diagnosis. Further health economic, performance and implementation studies are now required to assess the viability of offering these alternatives in routine clinical care.

Funding

Funding for this study was provided by the Health Technology Assessment programme of the National Institute for Health Research.

Health Technology Assessment

HTA/HTA TAR

ISSN 1366-5278 (Print)

ISSN 2046-4924 (Online)

Impact factor: 3.819

Health Technology Assessment is indexed in MEDLINE, CINAHL, EMBASE, The Cochrane Library and the Clarivate Analytics Science Citation Index.

This journal is a member of and subscribes to the principles of the Committee on Publication Ethics (COPE) (www.publicationethics.org/).

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This report

The research reported in this issue of the journal was funded by the HTA programme as project number 14/168/02. The contractual start date was in May 2016. The draft report began editorial review in June 2018 and was accepted for publication in February 2019. The authors have been wholly responsible for all data collection, analysis and interpretation, and for writing up their work. The HTA editors and publisher have tried to ensure the accuracy of the authors' report and would like to thank the reviewers for their constructive comments on the draft document. However, they do not accept liability for damages or losses arising from material published in this report.

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