

Prenatal and Obstetric Parameters of Late Terminations: A Retrospective Analysis

Pränatale und geburtshilfliche Parameter von Spätabbrüchen: eine retrospektive Analyse



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ABSTRACT

Background In Germany, the highly sensitive issue of late terminations of pregnancy and feticide is regulated in Sec. 218a para. 2 of the German Penal Code (medical indication). This study aimed to investigate the prenatal obstetric approach after feticide and the rate of maternal complications.

Material and Methods All feticides of singleton pregnancies carried out at Leipzig University Hospital (n = 164) in the period between 01/2016 and 12/2019 were retrospectively analyzed. Selective feticides of multiple pregnancies were excluded from the study. Target indicators for the prenatal obstetric approach were sonographic accuracy of estimation, method used to induce feticide, time between feticide and delivery, and whether curettage was required. The rate of maternal complications was defined as blood loss of ≥ 500 ml.

Results The number of feticides as a percentage of the total number of births during the investigation period was 1.6%. None of the terminations were performed primarily because of a serious risk to the mother's physical health; all of the indications to terminate the pregnancy were based on the psychosocial burden and the risk to the mother's mental health as outlined in Sec. 218a StGB (German Penal Code). The most common fetal diagnoses in the context of a maternal psychosocial emergency were central nervous system abnormalities (29.3%), numerical chromosomal aberrations (29.3%) and structural chromosomal aberrations/syndromes (21.3%). Sonographic measurements were used to estimate fetal weight and the weight of around half of the fetuses was underestimated (-121.8 ± 155.8 g). The margin of estimation error increased with increasing gestational age ($p < 0.001$). Misoprostol was the most common drug administered to induce labor. No significant association was found between the method chosen for induction, parity, fetal birth position, fetal anomaly, fetal gender, birth mode or the number of previous cesarean sections and Δ delivery. However, a significantly higher loss of blood was observed with longer Δ delivery ($p = 0.02$). The likelihood of requiring curettage increased with increasing loss of blood. The number of maternal complications as a percentage of the total patient population was 10.4%. Only 11% of patients agreed to a postmortem examination.

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Conclusion Late terminations of pregnancy carried out in accordance with Sec. 218a para. 2 StGB are a reality and must be understood and accepted as a possible consequence of modern prenatal medicine. The complication rate after feticide and the subsequent obstetric procedure was 10% for the above-defined maternal complication. Late terminations and their obstetric management should be carried out in specialized perinatal centers which offer interprofessional expertise.

ZUSAMMENFASSUNG

Hintergrund In Deutschland ist das hochsensible Thema Spätabbruch und Fetozid durch § 218a Abs. 2 StGB (medizinische Indikation) gesetzlich geregelt. Ziel dieser Studie war die Untersuchung des pränatal-geburtsmedizinischen Vorgehens nach Fetozid sowie der maternalen Komplikationsrate.

Material und Methoden Im Zeitraum zwischen 01/2016–12/2019 wurden retrospektiv alle am Universitätsklinikum Leipzig durchgeführten Fetozide bei Einlingsschwangerschaften ($n = 164$) analysiert. Selektive Fetozide bei Mehrlingschwangerschaften wurden ausgeschlossen. Als Zielgrößen des pränatal-geburtshilflichen Vorgehens galten die sonografische Schätzgenauigkeit, die Einleitungsmethode, das Zeitintervall zwischen Fetozid und Entbindung sowie die Notwendigkeit einer Kürettage. Die maternale Komplikationsrate wurde definiert als Blutverlust ≥ 500 ml.

Ergebnisse Der prozentuale Anteil der Fetozide an der Gesamtgeburtenrate im Untersuchungszeitraum betrug 1,6%. Es erfolgte kein Spätabbruch aufgrund einer primär physischen Gefährdung der Mutter, vielmehr wurden alle Indikationen ausschließlich aufgrund einer psychosozialen Belastung

und seelischen Gefährdung im Sinne des § 218a StGB gestellt. Die häufigsten Diagnosen im Kontext der psychosozialen Not-situation der Mutter waren ZNS-Auffälligkeiten (29,3%), numerische Chromosomenaberrationen (29,3%) sowie strukturelle Chromosomenaberrationen/Syndrome (21,3%). Bei etwa der Hälfte der Feten wurde das fetale Gewicht sonografisch unterschätzt ($-121,8 \pm 155,8$ g), wobei der Schätzfehler mit zunehmenden Gestationsalter zunahm ($p < 0,001$). Miso-prostol war das am häufigsten eingesetzte Medikament zur Weheninduktion. Es konnte kein signifikanter Zusammenhang zwischen der gewählten Einleitungsmethode, Parität, fetal-ten Lage, fetalen Anomalie, dem kindlichen Geschlecht, Geburtsmodus oder der Anzahl der vorangegangenen Sectiones caesareae zu Δ Entbindung gezeigt werden. Allerdings konnten mit einem zunehmenden Δ Entbindung signifikant höhere Blutverluste beobachtet werden ($p = 0,02$). Mit steigendem Blutverlust nahm die Wahrscheinlichkeit der Notwendigkeit einer Kürettage zu. Der Anteil maternaler Komplikationen am Gesamtkollektiv betrug 10,4%. Lediglich 11% stimmten einer Obduktion zu.

Fazit Spätabbrüche gemäß § 218a Abs. 2 StGB stellen eine Realität dar und müssen als mögliche Konsequenz der modernen Pränatalmedizin verstanden und getragen werden. Der Fetozid und das folgende geburtsmedizinische Prozedere waren, nach oben definierten Komplikationskriterien, mit einer Rate von 10% assoziiert. Die Durchführung von Spätabbrüchen sowie deren geburtshilfliches Management sollten an spezialisierten Perinatalzentren mit interprofessioneller Expertise erfolgen.

Abbreviations

CMV	cytomegalovirus
CNS	central nervous system
GW	weeks of gestation
s/p	status post
StGB	Strafgesetzbuch = German Penal Code
vs.	versus

Introduction

Almost no other prenatal obstetric topic is as polarized and discussed so controversially and emotionally as feticide, which is defined as the targeted killing of one or more fetuses in the womb [1]. From a gestational age of ≥ 20 –22 weeks of gestation (GW) or with the start of the fetus' viability [2], feticide is one of the options for late termination of a pregnancy to avoid the birth of an infant requiring high levels of medical care [3]. An intracardiac injection of potassium chloride is administered under sonographic control to induce fetal circulatory arrest.

As in many other countries, parental requests to terminate a pregnancy and feticide are highly sensitive topics in Germany. Hospitals do not hold uniform views on this issue, and this can be an additional psychological burden for affected patients.

The percentage of feticides of singleton pregnancies out of the overall number of pregnancy terminations has remained constant for several years at 0.6%. In 2018, a total of 641 feticides were carried out [4]. Legally, carrying out feticide in Germany is regulated in Sec. 218a para. 2 of the German Penal Code (medical indication). It states: "A termination which is performed by a physician with the consent of the pregnant woman is not unlawful if, considering the pregnant woman's present and future circumstances, the termination of the pregnancy is medically necessary to avert a danger to the life or the danger of a serious impairment to the pregnant woman's physical or mental health, and the danger cannot be averted by other means that would be reasonable for her to accept." [5]. The most common causes cited in the literature for this type of psychosocial emergency experienced by pregnant women are very severe fetal abnormalities and/or genetic findings (e.g., trisomies). The most common abnormalities are chromosomal aberrations, structural CNS abnormalities, structural heart defects, and multiple malformations [6, 7]. The Austrian Society of Pre- and Perinatal Medicine therefore describes feticide as a humanitarian, ethical, medical and legal form of late termination of pregnancy [8]. The statement by the German Board and College of Obstetrics and Gynecology (GBCOG) on the termination of pregnancy additionally states that the "danger to the life and health of the pregnant woman, as well as to her social and psychological health, [can] be a justi-

fication for assisting in a termination of pregnancy, [...] as no embryo or fetus can be saved in opposition to the mother” [9].

Couples who are confronted with a diagnosis of severe fetal abnormalities detected at a late gestational age usually face a moral and ethical dilemma and are under extreme psychological pressure. The problem is compounded by the fact that, in many places, hospitals are opposed to carrying out feticide, describing the procedure as a violation of medical ethics [10], as “autogenocide” [11] or “early euthanasia” [12].

Prenatal medical examinations, which are available across all of Germany, are important in any discussion of feticide. As the author A. Braun aptly states in her article, patients wishing to have a prenatal diagnostic workup should be aware already prior to any prenatal examinations what the consequences of potentially detecting fetal abnormalities could be for them [12]. This is a question that physicians providing prenatal care should also ask themselves, as the physician’s responsibility is not limited to the prenatal diagnostic workup (ultrasound, invasive, non-invasive examinations) but also covers the consequences, which may potentially mean, after extensive neutral counseling about the findings, that the parents request that the pregnancy be terminated or feticide carried out.

The data and number of available studies on this topic are limited. In clinical practice, we have often observed that the clinical management after feticide, the time to the stillbirth, postpartum complications such as increased bleeding, as well as the time spent in hospital are matters which particularly interest patients. The aim of this study was therefore to provide affected women with better advice about prenatal obstetric approaches and possible complications by evaluating data from the last five years.

Methods

Study design

A total of 164 feticides of singleton pregnancies were carried out at Leipzig University Hospital in the investigation period between 01/2016 and 12/2019 and were retrospectively analyzed. Selective feticides ($n = 1$) were excluded because of the independently increased risk of maternal bleeding in multiple pregnancies. In addition, one patient with an abnormally invasive placenta (s/p cesarean section), in whom the fetus and placenta were delivered after six weeks following a two-stage approach with preservation of the uterus, was also excluded from the study.

The data on the target criteria for the prenatal obstetric approach (accuracy of sonographic estimation, initial method used to induce labor, time between feticide and delivery, time spent in hospital, and if curettage was necessary) were retrospectively collected from electronic patient files. Additional data including gravidity, parity, maternal age, gestational age at delivery, birth weight and fetal diagnosis underpinning the mother’s psychosocial emergency were recorded.

The delivered fetuses were categorized into stillbirths (weighing ≥ 500 g or < 500 g but aged ≥ 23.0 GW) and miscarriages (< 500 g) in accordance with Sec. 31 of the German Civil Status Ordinance (PStV) [13].

Accuracy of sonographic estimation was defined as the difference between the estimated fetal weight (using the Hadlock I formula [14], with the ultrasound measurement carried out a maximum of seven days previously, GE E8/E10 type ultrasound device, Logiq Book [GE Healthcare, Little Chalfon, United Kingdom]) and the actual birth weight. To categorize the accuracy of estimation, deviations from the actual birth weight ± 100 g were defined as “accurate”, estimations which deviated by more than $+ 100$ g as “overestimation” and estimations which deviated by more than $- 100$ g as “underestimation”. The sonographic estimation was carried out by an experienced physician with an ultrasound experience of at least DEGUM II.

The time between feticide and delivery is referred to herein after as Δ delivery. The rate of maternal complications was defined as a blood loss of ≥ 500 ml. Whether the patient additionally required curettage for incompletely delivered placenta or following manual removal of a retained placenta was also recorded.

Multiprofessional management and procedure used for late termination

In Central Germany (Saxony, Saxony-Anhalt and Thuringia), the majority of feticides carried out in accordance with Sec. 218a para. 2 of the German Penal Code are carried out in the Obstetric Department of Leipzig University Hospital.

If severe fetal abnormalities are detected during the prenatal diagnostic workup, the parents are offered multidisciplinary, open-ended, neutral counseling about treatment options, available support and alternatives. This includes counseling by a neonatologist, often also by a pediatric surgeon and a psychologist and, in cases with CNS malformations, by a neurosurgeon or pediatric neurologist. The prenatal diagnostic findings are supplemented by a fetal MRI to confirm the detected pathologies and obtain a better assessment of the severity of the abnormality. The mother also receives genetic counseling. The decision to carry out feticide must be supported both by the parents and by the physicians carrying out the procedure.

Feticide is carried out from week 21.0 of gestation when the fetal weight should be > 500 g; if the gestational age is not clear or the fetus appears more mature on ultrasound imaging, the procedure may be carried out earlier. After prior administration of a weight-adapted fetal anesthesia consisting of midazolam, fentanyl, thiopental or mivacurium chloride, fetal circulatory arrest is induced by administration of an intracardiac, or in rare cases intravascular, injection of potassium chloride and recorded on camera (Viewpoint, GE Healthcare).

A medical autopsy is carried out postmortem in each case; in some cases, the dead infant is additionally examined by a medical doctor. A death certificate (cause of death: non-natural) must be issued for stillborn children (≥ 500 g). The entire procedure is reviewed by the public prosecutor’s office. A medical autopsy is always recommended but the final decision whether to have an autopsy or not lies with the parents. A babygram, i.e., a full-body radiological survey of the fetus, is proposed in cases with skeletal dysplasia. Although miscarriages (< 500 g), at least in Saxony and the neighboring German federal states of Thuringia, Saxony-Anhalt and Bavaria, are not subject to German burial law [15], these

► **Table 1** Description of the study population (n = 164) based on different categorical features. The number of feticides in the investigation period doubled because of the increased demand by patients living in Central Germany (above all, from Saxony-Anhalt).

	(%)	n
Calendar year		
▪ 2016	15.9/1.0*	26
▪ 2017	21.3/1.3*	35
▪ 2018	30.5/1.8*	50
▪ 2019	32.3/2.0*	53
Amniocentesis	82.9	136
Fetal gender		
▪ female	45.7	75
▪ male	53.0	87
▪ unknown	1.2	2
S/p cesarean section		
▪ no	86.0	141
▪ s/p cesarean section	12.2	20
▪ ≥ s/p repeat cesarean section	1.8	3
S/p cesarean section and initial method of induction		
▪ balloon catheter	21.7	5
▪ Cergem (1 g)	43.5	10
▪ Cervidil (1 g)	34.8	8
Parity		
▪ 0	42.7	70
▪ 1	40.2	66
▪ 2	8.5	14
▪ ≥ 3	8.5	14
Delivery method		
▪ spontaneous	98.2	161
▪ vaginal-surgical	1.2	2
▪ selective abdominal delivery	0.6	1
Blood loss (ml)		
▪ < 500	84.1	138
▪ 500–1000	7.3	12
▪ > 1000	3.1	5
▪ unknown	5.5	9
Curettage		
▪ total	18.3	30
▪ ≥ 500 ml blood loss	82.4	14
Autopsy	11.0	18

* Percentage of feticides out of the total number of births in the respective calendar year.

infants, often referred to as “butterfly babies” are often buried in cemeteries [16].

Parents are given psychological support and care during the entire time spent in hospital (prepartum and postpartum). This also includes the option of post-hospital outpatient talking ther-

apy and information about psychological drop-in centers and support groups located near the parent's place of residence, including parent-led support groups and postnatal groups for parents whose children died.

Induction of labor

Internationally, the drugs and methods used to induce labor are vary greatly [17]. The drug usually used at Leipzig University Hospital to induce late terminations is misoprostol (Cytotec®), applied vaginally at a dose of 800 µg (first dose), followed by oral administration of 400 µg every 4 hours thereafter. Lower oral doses of 25–50 µg are used when the gestational age of the fetus is more advanced or the fetus is older than 30 weeks of gestation. However, the administration of a synthetic prostaglandin E1 derivative such as misoprostol is completely contraindicated in women who are status post cesarean section because of the higher risk of rupture [18]. The treatment for these patients therefore consists of the application of 1 mg gemeprost (Cergem®) in the form of a vaginal suppository with repeated administration every 4 hours. Mechanical methods such as double-balloon catheter which can be filled either in the uterus or the vagina with up to 80 ml of saline solution are also used and left up to 24 hours in situ [17]. Mechanical methods alone are often insufficient to induce labor and need to be complemented by the addition of other methods during the procedure. For example, by the addition of 0.5 mg dinoprostone (Prepidil®), which is applied every 6 hours in the form of an intracervical gel. Alternatively, 1 mg of the prostaglandin E2 derivative Cervidil® (active agent dinoprostone) can be administered every 4 hours up to the maximum daily dose.

Statistical data analysis

Statistical analysis was carried out using the IBM Statistical Package for the Social Sciences (IBM SPSS V.24). Standardized statistical methods were used for analysis. The level of significance for all tests was 5% ($\alpha = 0.05$). Non-normally distributed means and ordinal data were compared using the Mann-Whitney U test and the Kruskal-Wallis test. The relationship between variables was examined using Pearson χ^2 -test and correlation analysis.

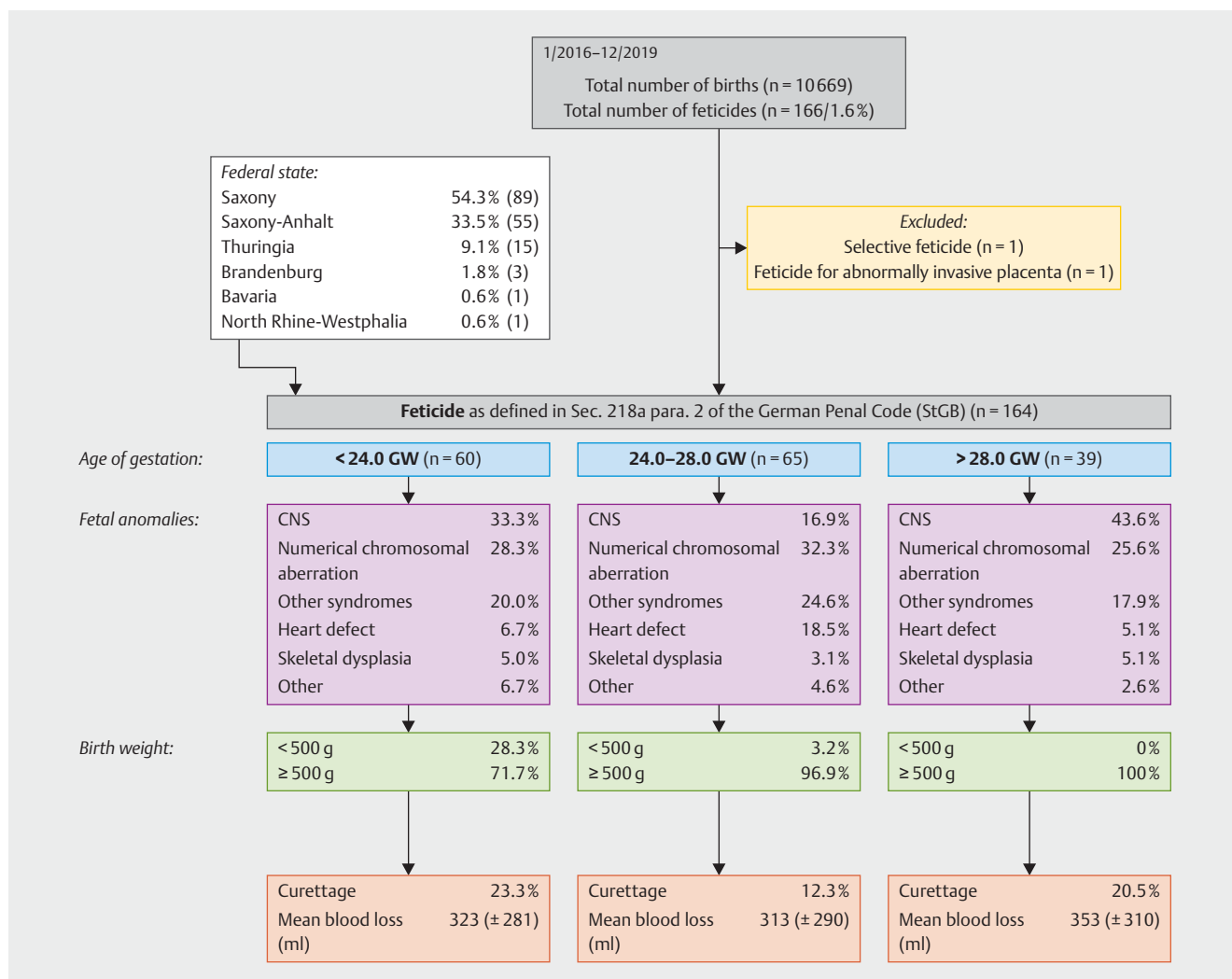
Ethics

Written consent for the scientific use of anonymized data is obtained from every patient as a standard practice at our institution. All procedures complied with the ethical standards of the committee responsible for human experiments (institutional and national) and the current version of the Declaration of Helsinki (1975). The study was approved by the ethics committee of Leipzig University Hospital (IRB00001750; reg. no. 310/20-ek).

Results

Description of the study population

A total of 164 cases with fetuses aged between week 21.5 and 36.2 of gestation were included in the analysis. The mean gestational age of the total fetal cohort at the time of delivery was 26.1 GW. The latest feticide was carried out in week 36.2 of gestation in a mother giving birth to her third child. A severe cerebral mal-



► **Fig. 1** Description of the study population grouped according to the gestational age of the fetus. A total of 166 feticides as defined in Sec. 218a para. 2 of the German Penal Code were carried out during the investigation period (01/2016–12/2019).

formation with agenesis of the corpus callosum, interhemispheric cysts, and pronounced migration and gyration disorders was detected in the fetus at a very late stage of pregnancy (diagnosis: 35.2 GW), which was only detected very late on neuroimaging.

The number of feticides carried out at Leipzig University Hospital doubled during the investigation period from 26 (in 2016) to 53 (in 2019), which in the final year amounted to 2.0% of the overall birth rate (► **Table 1**). Only around half of the patients (n = 89) were resident in the federal state of Saxony (54.3%); 40 of them (45.0%) came from Leipzig or the surrounding area. The majority of other patients came from the federal states of Saxony-Anhalt (n = 55; 33.5%) and Thuringia (n = 15; 9.1%) (► **Fig. 1**).

► **Table 1** describes the composition of the total study population. Around 83% (136/164) of the pregnant women asked for an invasive prenatal diagnostic workup by amniocentesis for a genetic investigation of potential abnormalities. Only 11% (18/164) agreed to a medically recommended autopsy (► **Table 1**). ► **Table 2** shows the categorical features of the study population grouped

according to gestational age (<24.0 GW n = 60; 24.0–28.0 GW n = 65; >28.0 GW n = 39). The mean birth weight was 941 g (± 558). On average, even fetuses aged <24.0 GW weighed more than 500 g (555 ± 118 g) (► **Table 3**).

Fetal malformations and time between diagnosis and feticide

The most common fetal anomalies were CNS abnormalities (29.3%), numerical chromosomal aberrations (29.3%), and structural chromosomal aberrations/syndromes (21.3%). The most common CNS abnormalities were complex cerebral malformations, agenesis of the corpus callosum, severe hydrocephalus, spina bifida, and congenital infections with CNS manifestation (toxoplasmosis, CMV). Numerical chromosomal aberrations consisted of trisomy 21 (56.3%), trisomy 18 (14/48; 29.2%), trisomy 13 (3/48; 6.2%) and “others” (4/48; 8.3%). Cardiac malformations (hypoplastic left or right heart syndrome, transposition of the great arteries, complex cardiac defects) were found in 11.0% of fetuses

► **Table 2** Description of the study population based on different categorical features. The table shows the results for the total study population (n = 164) as well as for the individual groups grouped according to gestational age (< 24.0 GW n = 60; 24.0–28.0 GW n = 65; > 28.0 GW n = 39).

	Total, % (n)	< 24.0 GW, % (n)	24.0–28.0 GW, % (n)	> 28.0 GW, % (n)
Fetal anomalies				
▪ CNS	29.3 (48)	33.3 (20)	16.9 (11)	43.6 (17)
▪ heart defect	11.0 (18)	6.7 (4)	18.5 (12)	5.1 (2)
▪ numerical chromosomal aberrations	29.3 (48)	28.3 (17)	32.3 (21)	25.6 (10)
▪ structural chromosomal aberrations	21.3 (35)	20.0 (12)	24.6 (16)	17.9 (7)
▪ skeletal dysplasia	4.3 (7)	5.0 (3)	3.1 (2)	5.1 (2)
▪ other	4.9 (8)	6.7 (4)	4.6 (3)	2.6 (1)
Sonographically estimated fetal weight				
▪ correct (< ± 100 g)	47.6 (78)	61.7 (37)	50.8 (33)	20.5 (8)
▪ underestimated (> – 100 g)	47.6 (78)	35.0 (21)	44.6 (29)	71.8 (28)
▪ overestimated (> + 100 g)	3.0 (5)	1.7 (1)	4.6 (3)	2.6 (1)
▪ not specified	1.8 (3)	1.7 (1)		5.1 (2)
Initial induction method				
▪ misoprostol	82.3 (135)	81.7 (49)	86.2 (56)	76.9 (30)
▪ balloon catheter	4.3 (7)	0	4.6 (3)	10.3 (4)
▪ Cergem	6.1 (10)	8.3 (5)	4.6 (3)	5.1 (2)
▪ Cervidil	5.5 (9)	10.0 (6)	4.6 (3)	0
▪ Prepidil	1.8 (3)	0	0	7.7 (3)
Fetal position at delivery				
▪ cephalic presentation	62.2 (102)	56.7 (34)	56.9 (37)	79.5 (31)
▪ breech presentation	37.8 (62)	43.3 (26)	43.1 (28)	20.5 (8)

(► **Table 2**). ► **Fig. 1** shows the percentage distribution of fetal anomalies grouped according to gestational age. The most common causes of the mother's psychosocial emergency were CNS abnormalities detected at an advanced gestational age (> 28.0 GW). There was no significant association between the percentage distribution of fetal anomalies and gestational age ($p = 0.97$).

The intervals between the time when the fetal abnormality was diagnosed and the time when feticide was carried out differed significantly. The interval for the gestational age < 24.0 GW differed significantly both from the grouped gestational age of 24.0–28.0 GW ($p < 0.001$) and from the gestational age > 28.0 GW ($p = 0.001$) (► **Table 3**).

Errors of sonographic weight estimation

In around half of the fetuses, the sonographically estimated weight of the fetus was underestimated. It was correctly estimated in approximately 50% of cases. Fetal weight was only overestimated in 5/164 fetuses (► **Table 2**). The mean error of estimation was -121.8 g (± 155.8). 99.1% (114/115) of fetuses estimated to weigh $\geq 500 \text{ g}$ did indeed weigh $\geq 500 \text{ g}$ at birth; 50% (23/46) of fetuses estimated to weigh < 500 g ultimately weighed more than $\geq 500 \text{ g}$ and thus, by law, had to be buried in a cemetery. The percentage of stillbirths in the total study cohort was 88.4%.

The weight of 75% of fetuses aged > 28.0 weeks of gestation was underestimated (► **Table 2**). The estimation error increased

significantly with increasing gestational age ($p < 0.001$) (► **Table 3**). No correlation was found between accuracy of estimation and the type of fetal anomaly ($p = 0.25$). In three cases, no fetal weight estimation data was found retrospectively.

Induction of labor and time between feticide and delivery (Δ delivery)

The percentage distribution of the methods initially used to induce labor after feticide, grouped according to gestational age, is shown in ► **Table 2**. The most commonly used drug was misoprostol which was used in more than 82% of cases. Cergem was used most often in women who were s/p cesarean section (► **Table 1**). Compared to Cervidil, Prepidil (24.0 vs. 34.3 GW, $p = 0.01$) and double-balloon catheters (24.0 vs. 29.0 GW, $p = 0.02$) were used significantly more often in the later weeks of pregnancy (► **Table 4**). The method chosen to induce labor had no significant impact on Δ delivery ($p = 0.1$; ► **Fig. 3**) or the duration of hospital stay ($p = 0.16$).

The interval between feticide and delivery is shown in ► **Table 3**, grouped according to gestational age. For the total study population Δ delivery was 24.6 hours (± 17.8). For three patients, Δ delivery was ≥ 5 days (5 days, 6.5 days and 27 days, respectively). To keep the impact of the three extreme values as low as possible but still include them in the data analysis, a value of 120 hours was used for each of these three women. One patient refused to have labor induced after feticide and presented to hospital 27 days lat-

► **Table 3** Analysis of variance using the Kruskal-Wallis test for different features grouped by gestational age. The p-value is only shown if the difference is significant ($p < 0.05$) and refers to the variance to the next categorical group.

	Mean	SD	Min.	Max.	95% CI	z-value	p
Maternal age (years)	31.4	5.7	17.0	46.0			
Gestational age at delivery (GW)	26.1	3.3	21.5	36.2			
Estimation error (g)	-121.8	155.8	-758.0	199.0			
▪ < 24.0 GW (n = 60)	-75.4	86.7	-285.0	192.0	-97.8; -52.6		
▪ 24.0–28.0 GW (n = 65)	-100.6	138.9	-491.0	197.0	-135.0; -66.1	3.94	< 0.001
▪ > 28.0 GW (n = 39)	-233.7	210.5	-758.0	199.0	-303.9; -163.5	4.76	< 0.001
Neonatal birth weight (g)	940.6	558.2	260.0	3170.0			
▪ < 24.0 GW	554.8	117.5	370.0	990.0	524.5; 585.2	-5.73	< 0.001
▪ 24.0–28.0 GW	834.0	249.9	260.0	1520.0	772.1; 896.0	-5.58	< 0.001
▪ > 28.0 GW	1711.5	587.7	860.0	3170.0	1521.0; 1902.0	-10.48	< 0.001
Time between diagnosis and feticide (d)	20.1	13.7	5.0	70.0			
▪ < 24.0 GW	14.0	9.4	5.0	55.0	11.6; 16.4	-4.81	< 0.001
▪ 24.0–28.0 GW	23.0	12.2	6.0	55.0	20.0; 26.1		
▪ > 28.0 GW	24.5	18.2	7.0	70.0	18.6; 30.4	-4.54	0.001
Time between feticide and delivery (h)	24.6	17.8	5.0	120*			
▪ < 24.0 GW	21.5	16.4	7.0	120*	17.2; 25.7		
▪ 24.0–28.0 GW	25.6	19.6	5.0	120*	20.7; 30.5		
▪ > 28.0 GW	27.6	16.4	6.0	72.0	22.3; 32.9	-2.56	0.03
Blood loss (ml)	326.3	290.8	100.0	2000.0			
▪ < 24.0 GW	323.2	280.8	100.0	1500.0	245.6; 400.6		
▪ 24.0–28.0 GW	312.7	290.4	100.0	2000.0	239.6; 385.8		
▪ > 28.0 GW	352.6	310.1	150.0	1600.0	252.0; 453.1		
Time spent in hospital (d)	2.5	1.2	1	11			
▪ < 24.0 GW	2.3	1.1	1	9	2.0; 2.6		
▪ 24.0–28.0 GW	2.4	1.4	1.0	11.0	2.1; 2.8		
▪ > 28.0 GW	2.8	1.0	1.0	6.0	2.4; 3.1	-2.41	0.048

SD: standard deviation, Min.: minimum, Max.: maximum, 95% CI: 95% confidence interval, g: grams, d: days, h: hours, ml: milliliters

* When the value for Δ delivery was ≥ 5 days, a raw value of 120 hours was used for the calculation to qualify the impact of extreme values.

This approach was used for three patients (respective times: 5 days, 6.5 days and 27 days).

er with spontaneous start of labor. A secunda gravida who was s/p cesarean section required a minor abdominal c-section in week 26.2 of gestation after 5 days of unsuccessful attempts to induce labor.

No significant correlation was found between parity ($p = 0.69$), fetal position at delivery (cephalic presentation/breech presentation) ($p = 0.61$), fetal anomaly ($p = 0.88$), neonatal gender ($p = 0.78$), mode of delivery ($p = 0.1$) or number of cesarean sections ($p = 0.60$) and Δ delivery. A higher neonatal birth weight ($r^2 = 0.18$; $p = 0.03$) or gestational age ($r^2 = 0.20$; $p = 0.01$) was found to be correlated with a significantly a longer Δ delivery (► **Table 4, Fig. 2**). Mean values for neonatal birth weights and gestational ages grouped for Δ delivery are shown in ► **Table 4**, although after categorization the only significant difference correlated with gestational age was Δ delivery < 24 hours vs. > 48 hours.

Maternal complications

The percentage of maternal complications (blood loss ≥ 500 ml) was 10.4% (17/164). The mean loss of blood for the total study population was 326.3 ml (± 291) and ranged from 100 ml to 2000 ml. 89% (138/164) of patients had a blood loss of < 500 ml. 7.7% (12/164) of patients had a blood loss of 500–1000 ml, and 3.2% (5/164) had a blood loss of > 1000 ml (► **Table 1**). No data on the amount of blood lost were available for 9 patients. It can be assumed that, given the lack of data on this point in these women, their blood loss was negligible. No significant differences in the amount of blood lost were found between the three subgroups grouped according to gestational age ($\chi^2 = 1.75$; $p = 0.42$) (► **Table 3**). Blood loss was also found not to be correlated with parity ($p = 0.97$) or the method used to induce labor ($p = 0.97$). However, it was found that a longer induction of labor (time between feticide and delivery) resulted in a significantly higher loss of blood ($z = -2.65$; $p = 0.02$). The mean hospital stay after a

► **Table 4** Correlations between two (independent) variables according to the Mann-Whitney U-test and Kruskal-Wallis test. p-values were only shown when the difference was significant ($p < 0.05$) and refer to the variance to the next categorical subgroup.

Correlation between two variables	Characteristics	Mean	SD	Min./Max.	p
Blood loss (ml) – curettage	no curettage (n = 134)	240.7	131.6	100/1200	< 0.001
	curettage (n = 30)	698.3	460.0	200/2000	< 0.001
	curettage + blood loss ≥ 500 ml (n = 14)	1046.4	441.4	600/2000	
Δ delivery (h) – blood loss	500–1000 ml (n = 12)	18.9	10.5	8/47	0.02
	> 1000 ml (n = 5)	54.6	41.8	21/120	
Duration of hospital stay (d) – blood loss	< 500 ml (n = 138)	2.4	1.1	1/11	0.04
	> 1000 ml (n = 5)	4.8	2.7	3/9	
Birth weight (g) – Δ delivery	< 24 hours (n = 111)	873	537.1	260/3170	
	24–48 hours (n = 41)	1038.5	550.8	400/2590	
	> 48 hours (n = 12)	1226.7	676.8	480/2490	
Gestational age at delivery (GW) – Δ delivery	< 24 hours (n = 111)	25.4	3.1	21.5/36.2	
	24–48 hours (n = 41)	26.6	3.6	21.6/35.5	
	> 48 hours (n = 12)	28.0	3.6	23.3/35.0	0.03
Gestational age at delivery (GW) – initial induction method	misoprostol (n = 135)	26.0	3.2	21.5/35.5	
	Cergem (n = 10)	25.0	2.3	22.6/28.4	
	Prepidil (n = 3)	34.3	3.2	30.6/36.2	0.01
	Cervidil (n = 9)	24.0	0.8	22.3/25.1	0.02
	balloon catheter (n = 7)	29.0	2.8	25.6/33.1	

SD: standard deviation, Min.: minimum, Max.: maximum, g: grams, d: days, ml: milliliters

loss of blood of > 1000 ml was 4.8 days (± 2.7) and was therefore significantly longer than that of patients with a blood loss of < 500 ml (2.4 ± 1.1 days) (► **Table 4**, **Fig. 2**). None of the patients received a blood transfusion.

82.4% (14/17) of patients with a blood loss of > 500 ml required curettage (mean: 1046.4 ± 441 ml). The mean loss of blood in the cohort which did not have curettage was 240.7 ml (± 131.6) and thus significantly lower ($p < 0.001$) than for patients who required curettage (698.3 ± 460 ml) (► **Table 4**). Gestational age had no impact on whether curettage was required ($\chi^2 = 0.26$; $p = 0.61$).

No maternal childbirth injury requiring surgical care was recorded for any of the patients.

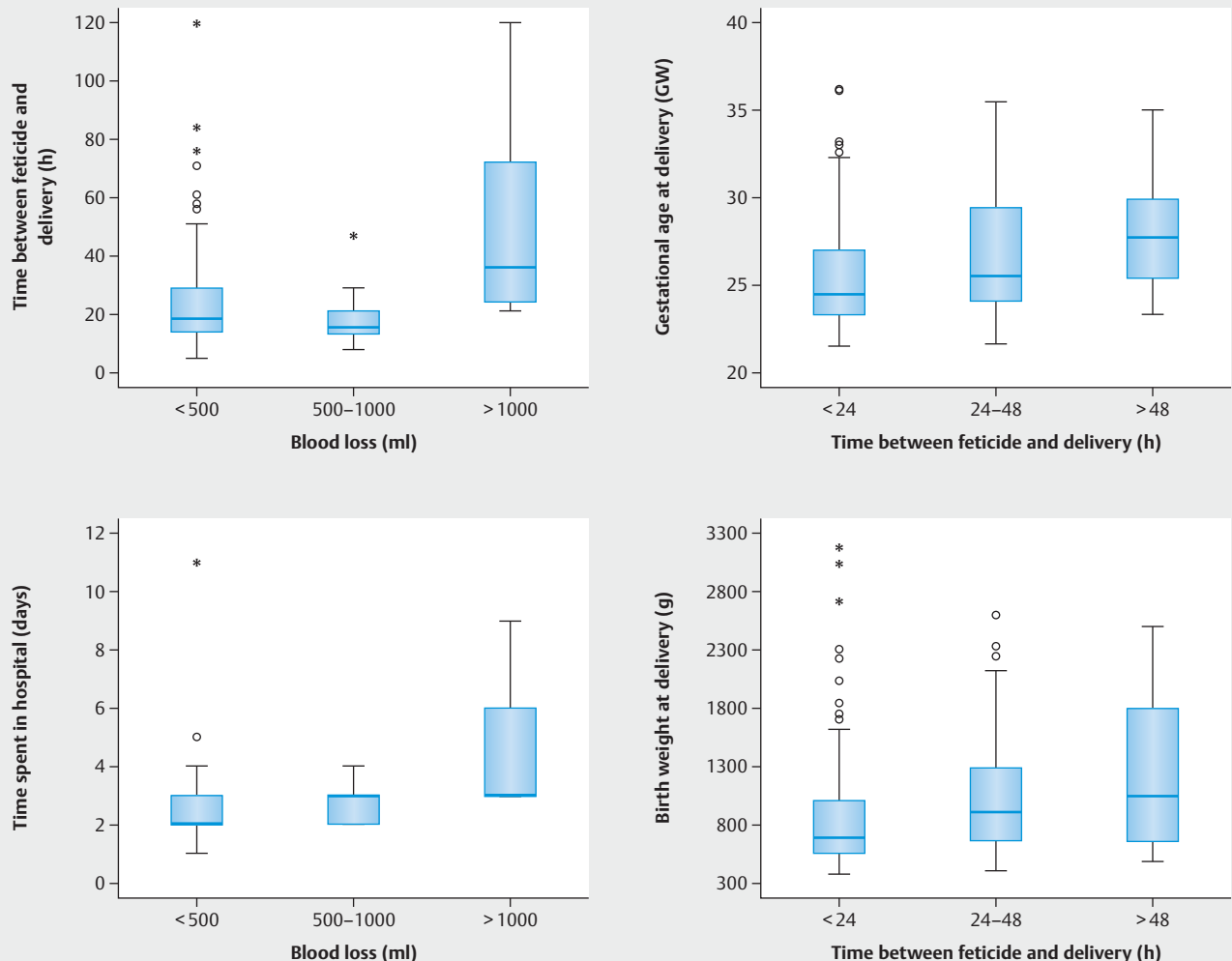
Discussion

Overall, there are only a few studies on obstetric management after feticide. There is no comprehensive study on this topic or this patient population or on maternal complications for Germany.

A late termination is carried out regularly (at least once a week) at Leipzig University Hospital, and this means that not only do the affected families face both emotional and organizational challenges, but the entire medical obstetric team does as well. According to figures obtained from the German Federal Statistical Office for 2018, 75% (51/68) of all feticides carried out in Central Germany (Saxony, Saxony-Anhalt, Thuringia) were carried out in Leipzig University Hospital [4]. In 2017, the percentage of pa-

tients resident in Saxony-Anhalt was well above the percentage of patients who lived in Saxony (45.7 vs. 31.4%). What affected pregnant women and families require is an infrastructure with nationwide provision of advisory and healthcare services which are available in appropriately identified centers. These centers should offer top-level prenatal diagnostic examinations and open-ended counseling of pregnant women, which would include explanations of all possible outcomes and their consequences (e.g., carrying the fetus to term followed by palliative care of the infant, maximum medical treatment of abnormalities diagnosed prenatally, or termination of the pregnancy).

When sonography is used to estimate fetal weight, an estimation error of ± 10 –15% is considered acceptable, although the Hadlock I formula we used is considered more precise compared to other formulas [19,20]. Based on the mean birth weight (941 g) and the mean error of estimation (-122 g), the accuracy of estimation for the investigated population was -13% . The accuracy of estimation is important for mothers of fetuses with an estimated fetal weight of around 500 g, as deceased infants with a birth weight of > 500 g must be buried in accordance with German burial law [14]. Visiting the grave can be an important part of coping with bereavement; other parents feel that by crossing the 500 g threshold, they face extreme organizational and financial challenges. Many couples want to know in advance which other developments they can expect to cope with after delivery, meaning that a change of category from miscarriage to stillbirth or the other way around places additional burdens on parents. In the



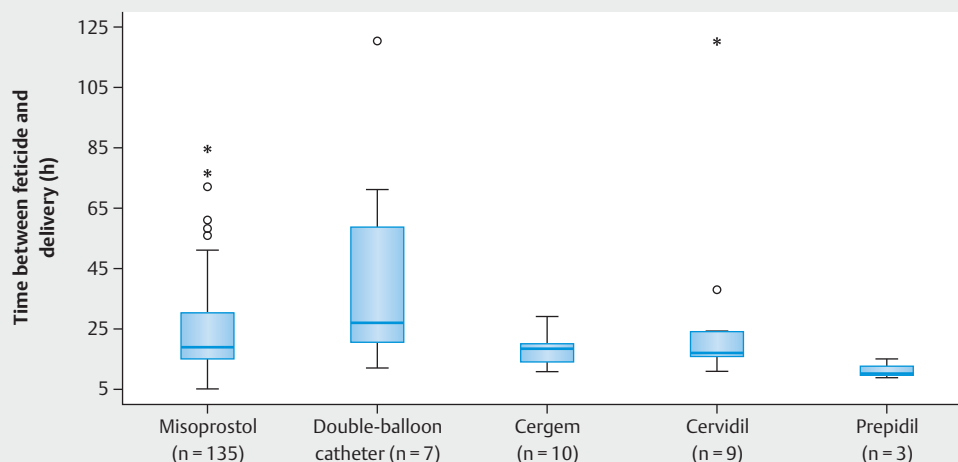
► **Fig. 2** Box plot of the most clinically relevant correlations for blood loss (ml) and time between feticide and delivery (h) for the group (n = 164). ° outliers, * extreme values.

end, 99% of fetuses estimated as weighing > 500 g, were, in fact, stillbirths.

In our study population, the mean time between the diagnosis and feticide was 20 days. In a review article from Gießen (n = 118) the reported interval between diagnosis and feticide was 17 days [21], which is comparable with our data. However, the mean age of gestation at Leipzig University Hospital was two weeks older (26.1 vs. 23.4 GW). This difference could be because our hospital's catchment area included more than one federal state. As, for various reasons, not all hospitals perform feticide [22], affected patients are forced to find a hospital which will do so; for organizational and diagnostic reasons this leads to a delay in carrying out the procedure, which places another unnecessary psychological burden on patients.

Most studies on late terminations focus on the methods used to induce labor. In our study, just as in the other studies, misoprostol was the most commonly used drug.

Our data did not show that misoprostol was superior to other drugs in terms of the time between inducing labor and delivery [3, 23, 24]. However, the regimens used by individual hospitals to induce labor vary greatly in terms of the dosages, mode of application (vaginal or oral) and intervals between application, making direct comparisons difficult. In general, administration of misoprostol resulted in delivery of the dead fetus within 17–24 hours, which corresponds to the results of our study (mean Δ delivery using misoprostol was 23.9 hours) [24–26]. The review article from Gießen reported a mean time between the start of induction and delivery of 2.6 days, although this was after prior cervical priming with prostaglandin [21]. Use of the drug mifepristone for cervical ripening, which increases endogenous production of and sensitivity to prostaglandin, can lead to a significant reduction in the administered doses of misoprostol and ultimately to a reduction of the time between the induction of labor and the birth [3, 27]. After the oral administration of mifepristone, patients are discharged home for 24–48 hours. As the catchment area of the pa-



► **Fig. 3** Box plot of the time between feticide and delivery (Δ delivery) according to the initial method used for induction. In a few cases ($n = 12$), the methods initially chosen to induce labor were supplemented by other methods during the procedure (e.g., double-balloon catheter and Prepidil). ° outliers, * extreme values.

tients who attend Leipzig University Hospital is very big and some patients have to drive for several hours to reach the hospital, this way of managing cervical ripening is difficult and is therefore not used at our hospital. Inpatient priming with mifepristone (24–48 hours) would hugely exceed the mean time to delivery after induction with misoprostol.

In general, the data showed that with regard to maternal health, late terminations are associated with low rates of maternal complications. Nevertheless, requests to Leipzig University Hospital to carry out the feticide on an individual basis with the mother subsequently giving birth at another site are rejected, as the focus at our hospital is to provide patients with integrated care and the actual feticide injection must not be viewed and carried out in isolation. Even though only 10% of patients lost ≥ 500 ml of blood (five cases lost between 1000–2000 ml of blood) and no other serious complications were observed, delivery should take place in specialized perinatal centers which have the necessary expertise (in particular, midwives assisting at the birth), psychological support and medical resources. In our study population, every 5th patient required curettage after delivery of the fetus. The main causes of blood loss were bleeding, although the analysis did not differentiate between atonic bleeding and bleeding caused by retained placental fragments. The reported rates of curettage in other studies on late terminations in the second and third trimesters of pregnancy ranged from 2.5% to 55% [27, 29, 30], although this difference can be ascribed to differences in obstetric management as, in other hospitals, curettage in the second trimester of pregnancy is the standard procedure.

The fact that ultimately only 11% of patients agreed to an autopsy was a surprising and not very satisfactory outcome, as autopsies are medically recommended. As the prenatal diagnosis was already definitive and any findings during the postmortem would have no impact on the decision for or against feticide, many patients who are already psychologically stressed [28] refuse to

have an autopsy to spare their infant (and themselves) from going through this procedure. Nevertheless, autopsies are an important instrument and should be preferred, as they serve as means of quality assurance for diagnostic examination and, in some cases, may be useful to detect additional issues and diagnoses which could have an impact on genetic counseling and the risk of recurrence [31, 32].

In its press release on terminations of pregnancy, the German Board and College of Obstetrics and Gynecology (GBCOG) stated pertinently that “*termination of a pregnancy [...] [is] unfortunately in some cases a necessary solution for an existing pregnancy conflict [which] [...] must be understood as a means of providing help to women in distress [...] and [...] must not be viewed as a social flaw. The medical profession is a mirror of our society, also with regard to personal attitudes towards terminations of pregnancy*” [9]. This discussion underlines the importance and responsibility of prenatal medicine, because prenatal diagnostic workups should not just fulfil the “*social desire for a perfect and ‘healthy’ child*” [12] but are also required to obtain a diagnosis and provide a basis for treatment, which means that feticide could be considered a potential consequence of carrying out prenatal diagnostic examinations. Nevertheless, termination of a pregnancy, irrespective of the age of gestation, “*will never be anything other than one of several bad options*.” [9].

Finally, it should be noted that this study only examined feticide and its management. A late termination is only one of several options after detecting severe fetal abnormalities. Another alternative is to carry the infant to term, and the infant then receiving highly competent, neonatal palliative care. This alternative is also discussed with parents at Leipzig University Hospital and is one of the available options. In every case, the loss of the child is an enormous emotional and psychological burden for affected couples, irrespective of what path (late termination vs. palliative care) they ultimately choose.

Conclusion

Late terminations and feticides as defined in Sec. 218a para. 2 of the German Penal Code are part of the practical reality of obstetrics and should be understood and accepted as a potential consequence of modern prenatal medicine. Carrying out a late termination of feticide must take account of the legal requirements, ethical and moral concerns, and the pregnant woman's and the doctor's right of self-determination. Comprehensive nationwide counseling and care services are necessary to provide the best possible support to couples in this extremely difficult situation and to forestall avoidable organizational problems (delay until the correct diagnosis is obtained). The data presented here should serve as a basis when counseling affected couples, as the data show that feticide and the subsequent obstetric procedure is associated with low maternal complication rates if the procedure is carried out in a specialized perinatal center. The preconditions for this are an interdisciplinary team with the relevant expertise and resources.

Conflict of Interest

The authors declare that they have no conflict of interest.

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