Society of Family Planning Clinical Recommendation: Induction of fetal asystole before abortion

Jointly developed with the Society for Maternal-Fetal Medicine☆,☆☆

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This document serves as a revision to the Society of Family Planning's 2010 guidelines, integrating literature on new techniques and research and addressing the clinical, medical, and sociolegal questions surrounding the induction of fetal asystole. Insufficient evidence exists to recommend routine induction of fetal asystole before previable medication and procedural abortion. However, at periviable gestations and after fetal viability, inducing fetal asystole before abortion prevents the infrequent but serious occurrence of unanticipated expulsion of a fetus with cardiorespiratory activity (Best Practice). Defining viability is complicated as it represents a physiological continuum impacted by gestational duration along with multiple other individual clinical factors and circumstances; therefore, the exact gestational duration to offer fetal asystole will depend on the setting and clinical circumstances. If induction of fetal asystole before abortion is available, we recommend engaging in patient-centered counseling regarding the risks and benefits of induction of fetal asystole in the setting of each unique pregnancy scenario and the patient's beliefs and priorities (Best Practice). We recommend that clinicians identify the optimal pharmacologic agent to administer for a given clinical scenario based on factors such as availability of each agent; the time frame in which fetal asystole needs to be established; and clinicians' technical ability, preferences, and practice (Best Practice). Potassium chloride, lidocaine, and digoxin are all acceptable pharmaceutical agents to induce fetal asystole before abortion. To establish asystole rapidly, we suggest the use of potassium chloride (via intracardiac or intrafunic injection) or lidocaine (via intracardiac or intrafunic injection) (GRADE 2C), although intrathoracic administration of lidocaine may be acceptable. We recommend potassium chloride not be used if intracardiac or intrafunic location cannot be achieved to avoid the risk of accidental administration to the pregnant individual and because insufficient data support its efficacy via other intrafetal locations (GRADE 1C). When using digoxin, we recommend intrafetal administration (GRADE 1C), although intraamniotic administration may be acceptable depending on a clinician's technical ability and setting. Because digoxin may take several hours to induce asystole, an alternative agent should be considered in settings where fetal asystole must be confirmed rapidly.

Keywords: Abortion, Digoxin, Fetal asystole, Feticide, Lidocaine, Potassium chloride

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1. Introduction

1.1. Purpose

In 2010, the Society of Family Planning released clinical guidance on the induction of fetal demise before abortion.[1] Over the past decade, new studies on the efficacy, safety, and dosing of the methods reviewed in the 2010 guidance have been published, as well as studies on newly employed pharmacologic and mechanical methods. This document serves as a revision to the Society of Family Planning's 2010 guidelines, integrating literature on new techniques and research and addressing the clinical, medical, and sociolegal questions surrounding inducing fetal asystole.

1.2. Epidemiology

Abortion is an essential component of reproductive healthcare.[2] In 2020, approximately one in five pregnancies in the United States ended in an abortion.[3] Methods of abortion, including medication and procedural abortion, are safe and effective in all trimesters.[4] In second- and third-trimester abortion, clinicians may employ techniques to induce and confirm fetal asystole before an abortion.[1,5]

1.3. Background

The first documented successful selective termination was done with intracardiac puncture by Aberg et al. in 1978.[6] Since then, studies have described the intrafetal and intraamniotic injection of various pharmacologic agents to induce fetal asystole both for multifetal pregnancy reduction and selective termination and for abortion. While other methods to induce asystole have also been employed and examined, such as mechanical techniques immediately preabortion, pharmaceutical injection is more commonly practiced and studied.[1,5]

1.4. Legal climate

Since 1973, when abortion was identified as a constitutional right in all 50 states by *Roe v. Wade*, there have been countless legal challenges to abortion provision and access.[7] These legal challenges culminated in the removal of the federal right to abortion by *Dobbs v. Jackson* in 2022.[7] As a result, clinicians who provide abortion care have been forced to navigate unscientific and hostile laws—adapting their evidence-based provision of health care to comply with the ever-changing legal landscape. This antagonistic environment varies widely by state, resulting in differing clinical practices across the country.[8]

Medical societies, including the Society of Family Planning, the Society for Maternal-Fetal Medicine, and the American College of Obstetricians and Gynecologists, oppose laws and regulations that interfere with the evidence-based practice of medicine.[9] The recommendations in this document are informed by evidence regarding clinical outcomes and patient preferences. Federal and state laws and institutional policies impact how abortion care is provided, including induction of fetal asystole before abortion.[10] Abortion is not legal in all states and circumstances. The purpose of this document is to prepare clinicians to provide abortion care in circumstances where it is legal. Given the sweeping impact of recent legislation and institutional policies on abortion care across the United States, clinicians should familiarize themselves with the laws and regulations that affect their practice or consult a lawyer.

1.5. Interpretation of the evidence

This Clinical Recommendation is based on a careful examination of available scientific data, supplemented with expert opinion when the evidence is limited. Conducting prospective, randomized control trials (RCTs) on inducing fetal asystole is particularly challenging given the variation in practice patterns, patient preference, and perceived clinical and legal risks, resulting in limited studies in the literature. The lack of published literature should not be interpreted as evidence against the utility of induction of fetal asystole before abortion.

Inducing fetal asystole is an important consideration with increasing gestational duration, particularly after fetal viability. The term fetal viability is used in this document to signify a period in which there is a reasonable expectation of sustained fetal survival outside the uterus. Defining viability is complicated as it represents a physiologic continuum impacted by gestational duration along with multiple other individual clinical factors and circumstance.[11] Periviability is the period when the fetus may survive outside the uterus with life-sustaining interventions with a high risk of death and severe morbidities.[12] After fetal viability, induction of fetal asystole prevents the infrequent but serious occurrence of unanticipated expulsion of a fetus with cardiorespiratory activity. However, because viability is multifactorial and there is no single factor that distinguishes previability, periviability, and viability, clinicians may still induce fetal asystole in the previable and periviable periods. Thus, it is crucial to consider the specific clinical context when assessing the need for inducing fetal asystole. Finally, differences in technical capabilities, patient groups, and access to resources will create acceptable variation in clinical practice. The evidence-based review and guidance in this document are intended to support clinical decision-making in a variety of settings, with the goal of maintaining the broadest access to safe abortion care.

2. Clinical Questions

2.1. What are the reasons clinicians may offer induction of fetal asystole before abortion?

Medication abortion

Some studies have examined the use of fetal asystole induction before medication abortion (formerly referred to as induction termination). Retrospective cohort studies of inducing fetal asystole before second-trimester medication abortion have reported a decrease in the induction-to-delivery interval.[13,14] One retrospective cohort study of 146 second-trimester pregnancies reported a nonsignificant 10.9-hour difference in the induction-to-abortion interval for patients who received intracardiac potassium chloride to induce fetal asystole compared with those who did not (53.8 hours and 42.9 hours, respectively).[15] Another retrospective cohort study of 144 patients with a mean gestational duration of 21.4 ± 4.5 weeks of gestation found a nonsignificant 3-

hour difference in duration of termination from initiation of oral misoprostol regimen to delivery in 99 patients who had fetal asystole induced with intracardiac potassium chloride compared with 45 who did not (35.4 hours and 32.4 hours, respectively).[16] These two studies consisted only of medication abortion for fetal anomalies. These studies used different medication abortion methods, including oral or vaginal misoprostol, prostaglandin E2 suppositories, Foley bulbs, and oxytocin, among other methods.

Clinicians report that blood flow to the uterus decreases quickly after fetal asystole, [17] though there is limited published evidence to support this. A single retrospective chart review of 15 persons undergoing medication abortion between 18 and 31 weeks of gestation with a complete placenta previa, six of whom received fetal intracardiac potassium chloride injections, suggested that blood loss may decrease with the use of intracardiac potassium chloride.[17] The patients who received intracardiac potassium chloride had a smaller decrease in their hemoglobin associated with the procedure compared with the patients who did not receive the injection and did not have fetal demise (1.0 g/dL vs 2.5 g/dL, $p = 0.03$).[17]

Insufficient evidence exists to recommend routine induction of fetal asystole before a previable medication abortion. However, at periviable gestations and after fetal viability, inducing fetal asystole before medication abortion prevents the infrequent but serious occurrence of unanticipated expulsion of a fetus with cardiorespiratory activity (Best Practice; Table 1). Defining viability is complicated, as it represents a physiological continuum impacted by gestational duration along with multiple other individual clinical factors and circumstances; therefore, the exact gestational duration to offer fetal asystole will depend on the setting and clinical circumstances.

Procedural abortion

One peer-reviewed RCT of induction of fetal asystole with the use of digoxin 1 mg intraamniotic vs placebo 1 day before procedural abortion via dilation and evacuation between 20 and 23 weeks of gestation demonstrated a nonsignificant difference in procedure duration (mean ± SD, digoxin 15.4 ± 8.0 minutes vs placebo 14.7 ± 7.0 minutes, $p = 0.60$) or physician-reported difficulty with the procedure (digoxin 2.5 vs placebo 3 on a scale of 0−5, $p = 0.64$).[18] This study had insufficient power to detect a difference in secondary outcomes of excessive blood loss, complications, or patient-reported pain.[18] It is important to note that intraamniotic digoxin takes longer to achieve fetal asystole than intrafetal digoxin, and the study did not document when fetal asystole occurred.

A retrospective cohort study of 291 procedural abortions between 18 and 24 weeks of gestation with potassium chloride and 257 without potassium chloride found a shorter procedure duration with intracardiac potassium chloride (12.7 vs 16.1 minutes, $p < 0.001$), which remained significant when controlling for other variables in a multivariate logistic regression model (3.5-minute shorter duration, 95% CI 2.4−4.6).[19]

In a survey of 105 family planning specialists, some clinicians anecdotally reported improved cervical priming, softening of fetal cortical bone, and ease of procedures at later gestational durations as benefits of inducing fetal asystole.[20] A case series of 1677 procedural abortions between 18 and 34 weeks of gestation (median of 22 weeks) describes the induction of fetal asystole with intrafetal digoxin 1 to 2 days before procedural abortion via dilation and evacuation resulting in cervical softening, dilation, effacement, and softening of products of conception.[21] The impact of the duration of fetal asystole before procedural abortion has not been examined in controlled studies.

Insufficient evidence exists to recommend routine induction of fetal asystole before a previable procedural abortion because it has not been shown conclusively to improve the ease of procedure or reduce complications during dilation and evacuation. However, at periviable gestations and after fetal viability, induction of fetal asystole before procedural abortion prevents the infrequent but serious occurrence of unanticipated expulsion of a fetus with cardiorespiratory activity (Best Practice).

2.2. Why may patients prefer induction of fetal asystole before abortion?

Patients may desire induction of fetal asystole before an abortion for many reasons, and their preferences also may be influenced by the counseling they receive and the practice patterns at the facility where they receive care. A qualitative study of 20 individuals undergoing

TABLE 1
Key for GRADE recommendations[a]

Symbol	Meaning
1	Strong recommendation
2	Weaker recommendation
A	High-quality evidence
B	Moderate quality evidence
C	Low-quality evidence, clinical experience, or expert consensus
Best Practice	Recommendation in which either (1) there is an enormous amount of indirect evidence that clearly justifies a strong recommendation, direct evidence would be challenging and inefficient use of time and resources to bring together and carefully summarize, or (2) a recommendation to the contrary would be unethical

[a] Society of Family Planning Clinical Recommendations use a modified GRADE system. The GRADE system is described in several publications, with a comprehensive set of articles in the Journal of Clinical Epidemiology (J Clin Epidemiology, (2011) 64:383-394, 64:395-400, 64:401-406, 64:407-415, 64:1277-1282, 64:1283-1293, 64:1294-1302, 64:1303-1312, 64:1311-1316, (2013) 66:140-150, 66: 151-157, 66:158-172, 66:173-183, 66:719-725, 66:726-735).

procedural abortion via dilation and evacuation at a clinic with routine digoxin administration reported that 60% (12/20) felt reassurance or more emotionally comfortable with procedural abortion via dilation and evacuation after receiving digoxin; at the same time, 45% (9/20) reported feeling difficulty or emotional discomfort with carrying a demised fetus.[22]

Most participants enrolled in an RCT of digoxin for inducing fetal asystole preferred injection of digoxin (92%) compared with not receiving digoxin.[18] Of the 107 participants who indicated they would prefer digoxin before procedural abortion via dilation and evacuation, the most common reasons cited were a preference for fetal death before procedural abortion via dilation and evacuation (35%) and a belief that it would make the procedure easier (29%).[18]

If induction of fetal asystole before abortion is available, we recommend engaging in patient-centered counseling regarding the risks and benefits of induction of fetal asystole in the setting of each unique pregnancy scenario and the patient's beliefs and priorities (Best Practice).

2.3. Does induction of fetal asystole have any benefit related to the fetal perception of pain during an abortion?

Current scientific evidence indicates that neurological development precludes fetal perception of pain during abortion before 29 to 32 weeks of gestation, rendering inducing fetal asystole of no benefit for this purpose.[23,24] For pain to be perceived, multiple areas of the brain must be involved. Withdrawal reflexes and the release of stress hormones previously have been used as evidence of fetal pain perception.[24] Throughout gestation, the nervous system develops and becomes substantially more complicated. A large systematic review from 2005 showed the connections between nerves receiving painful stimuli to the cerebral cortex were necessary for a fetus to perceive pain and did not occur until approximately 29 weeks of gestation at the earliest.[25] However, in more recent data, the concept of a "pain center" has been replaced with a dynamic "pain connectome," which recognizes that the conscious experience of pain arises from a network of brain activity.[26] These connections likely do not occur until later, beyond at least 32 weeks of gestation.[26,27] While connections may be present earlier, they likely do not generate a pain experience because cortical structures are not functionally connected until at least 29 to 32 weeks of gestation.[24]

2.4. What techniques are appropriate for the induction of fetal asystole?

Currently, most induction of fetal asystole is achieved via pharmaceutical injection.[1,5] Other approaches, such as cardiac puncture and exsanguination or air embolization, have been practiced in the past,[28,29] but this document will focus on pharmaceutical injection.

Pharmacologic agents to induce fetal asystole before procedural or medication abortion

Pharmacologic agents are the most common means to induce fetal asystole before abortion. The most widely used agents are digoxin, potassium chloride, and lidocaine (Tables 2 and 3), with the injections done under direct ultrasound guidance. Patient monitoring beyond vital signs before injection is not routinely recommended. Post injection, patient monitoring is not necessary for the asymptomatic patient.

Digoxin

Technique

Digoxin is a cardiac glycoside that inhibits the sodium-potassium ATPase. Clinicians have used digoxin to induce fetal asystole before abortion for several decades. Most published studies describe an ultrasound-guided transabdominal approach for intraamniotic digoxin administration[18,21,30–35], although there is documented success with transvaginal approach for intraamniotic digoxin administration.[36,37] Intrafetal digoxin administered either transvaginally or transabdominally has higher rates of success in inducing asystole.[30,31,36] Based on expert opinion, clinicians typically aim for the fetal thorax or calvarium with this technique.

Dose

Most evidence supports the use of digoxin 1 mg, which has been shown to be safe regardless of route of administration (see Table 2). Early studies used 1.5 or 2 mg.[21,32,34] One study found doses lower than 1.0 mg had higher failure rates.[32] Most studies do not compare dosage directly, except one study[38] that found no difference in efficacy between digoxin 1 mg and 1.5 mg.

Effectiveness

The reported success rate of digoxin to induce fetal asystole with first injection is variable, ranging from 77.0% to 99.4% by the next day.[36,38] From the current literature, intrafetal administration achieves asystole more consistently than intraamniotic injection. Most reports of intraamniotic digoxin administration document failure rates around 8% to 10%.[18,32,35,39] Other studies have shown higher rates of failure even with the same techniques.[38] One study found a 31% failure rate in transabdominal intraamniotic injection compared with a 4.7% failure rate with intrafetal placement.[32] Another study found a failure rate of 23% in intraamniotic injection compared to 15% with intrafetal injection of the same digoxin dose.[38] Because most studies assess the efficacy of digoxin injection by confirming fetal asystole several hours after the injection or the following day, there is a paucity of data on the precise time to asystole following digoxin administration. More data are needed to better understand how quickly digoxin induces asystole. No data compare the efficacy of injection within different fetal compartments.

Risks

Risks of digoxin injection to induce fetal asystole include superficial or intrauterine infection, delivery of the pregnancy before the abortion procedure (extramural delivery), and side effects, including nausea, vomiting, fatigue, and discomfort at the injection site. Digoxin is a cardiac glycoside that presents a risk of cardiotoxicity due to electrolyte abnormalities leading to arrhythmias if injected into circulation of the pregnant individual. In a study that reported cardiac monitoring and serum studies of patients after digoxin 1 mg

TABLE 2
Doses and techniques of pharmacologic agents used to induce fetal asystole

Agent	Injection route	Dosage range	Efficacy	Reported side effects	Notes
Digoxin	Intraamniotic	0.5–2 mg	77%–100%	Nausea, vomiting, cramping, extramural delivery	Digoxin is administered most commonly via transabdominal approach with intraamniotic placement, though intrafetal is also often used. 1 mg of digoxin is used most commonly. Time to demise is at least several hours, though no exact data have been collected on time to asystole. Nausea and vomiting are common side effects.
	Intrafetal	1–1.5 mg	85%–98.4%		
Potassium chloride	Intrathoracic	1 mL[a]	100%	Risk of cardiac toxicity with accidental maternal administration, extramural delivery	Potassium chloride is administered most commonly via transabdominal approach with intracardiac placement. Dosage ranges in the literature based on clinical practice, but most commonly 6 to 20 mEq is used. Time to demise is usually instantaneous. Few side effects have been reported; however, there is significant maternal cardiac risk if injected intravascularly.
	Intracardiac	3–40 mEq	95.5%–100%[b]		
	Intrafunic	2–20 mEq	86.7%–100%		
Lidocaine	Intracardiac or intrathoracic	50–480 mg	85.7%–97.9%	One case of mild tinnitus, no extramural delivery reported	Lidocaine is administered most commonly via transabdominal approach with intracardiac or intrathoracic placement. Doses range in the literature based on clinical practice, but most commonly 200 to 240 mg is used. Time to demise is usually within 5 minutes. No significant side effects have been reported.
	Intrafetal, transabdominal approach	200–240 mg	100%		
	Intrafetal, transvaginal approach	200–240 mg	61.3%		
	Intrafunic	70–300 mg	92%		

This table includes doses, routes, efficacy rates, and side effects documented in the published literature. More information on the studies including gestational age and sample size can be found in Table 3.

[a] Concentration of potassium chloride solution was not included in the report; [b] One outlier study documented only 57.9% efficacy of first injection (Chen 2009).

intraamniotic injection, investigators found no abnormal cardiac rhythms or changes in coagulation parameters in the pregnant individual.[33] A more recent study also examined serum levels of digoxin and electrocardiograms after 2 mg intraamniotic injections; digoxin levels were within therapeutic range, much below toxic levels, at 6, 10, and 20 hours after injection administration and patients' electrocardiograms were all unremarkable.[40]

One study reported that extramural deliveries occurred in 0.3% of a cohort of 4906 persons between 18 and 24 weeks of gestation who had received digoxin 1 mg via intraamniotic or intrafetal route.[41] Other extramural delivery rates with digoxin use have been reported from 0.5% to 5.6%, being highest with intraamniotic digoxin.[30–32] Not all studies specifically track extramural deliveries. Commonly known side effects of digoxin administration, such as nausea and vomiting, also are not always reported. Some postulate these symptoms may represent early signs of digoxin toxicity.[33] One study described rates of infection to be significantly higher with intraamniotic injection compared to intrafetal administration, with an overall infection rate of 3.4%,[30] while other studies report rates of infection from 0% to 1%.[21,36,41]

Challenges

Efficacy of fetal asystole with digoxin injection and the precise timing of fetal asystole is variable and difficult to evaluate, presenting challenges to confirming asystole and increasing risk of extramural delivery.

Potassium chloride

Technique

Potassium chloride induces asystole through the dysregulation of intracellular and extracellular potassium concentration in the cardiac myocytes. Early techniques focused on the use of potassium chloride for fetal reduction in multiple gestations,[42] largely with intrathoracic placement up to 14 weeks of gestation.[43–47] Studies describe intrafunic injection of potassium chloride at 14 0/7 weeks of gestation and later as the first step in procedural abortion via dilation and evacuation.[48–51] Most commonly, intracardiac potassium chloride is injected under ultrasound guidance transabdominally in a fetal cardiac ventricle where aspiration of fetal blood will confirm correct placement. It is usually

TABLE 3
Efficacy of pharmacologic agents used to induce fetal asystole

Authors	Year	Regimen	Dose	*N*	Gestation	First injection failure rate
Digoxin						
Molaei	2008	Intraamniotic	0.5–1 mg	1795	17–24	0%–8.3% (depending on dose)
Nucatola	2010	Intraamniotic	1 mg	13	18–24	8%
		Intrafetal	1 mg	13	18–24	8%
		Intraamniotic	1.5 mg	13	18–24	23%
		Intrafetal	1.5 mg	13	18–24	15%
Dean	2012	Intraamniotic and intrafetal	1 mg	583	18–24	Not reported
Steward	2012	Intraamniotic or intrafetal	1 mg	4906	18–24	Not reported
Gariepy	2013	Intraamniotic, transvaginal	1 mg	26	18–23.5	15.4%
Tocce	2013	Intraamniotic and intrafetal, transvaginal	Mostly 1 mg	1662	18–22	0.6%
White	2016	Intraamniotic	1 mg	132	20–24	19.9%
		Intrafetal	1 mg	136	20–24	1.6%
Sharvit	2019	Intraamniotic	2 mg	59	21–30	6.8%
Tufa	2020	Intraamniotic	1 mg	49	20–24+ (max gestation not specified)	10.2%
Sium	2022	Intraamniotic	1 mg	49	20–28	10.2%
Potassium chloride						
Senat	2002	Intrafunic	20 mEq	10	22–38	0%
Bhide	2002	Intracardiac	8–40 mEq	73	18–35	0%
Bhide	2002	Intrafunic	6–16 mEq	21	17–33	9%
Hern	2004	Intracardiac	6–40 mEq	5	32+	0%
Pasquini	2008	Intracardiac	6–10 mEq	239	20–36	0%
Chen	2009	Intracardiac	6 mmol	19	24–38	42%
Sfakianaki	2013	Intracardiac	3–40 mL	192	15–24	0.5%
Nippita	2021	Intrafunic	20 mEq	32	20–23	0%
Caypinar	2022	Intraventricular	3–8 mL	79	22–35	0%
		Interventricular septum	2–6 mL	79	22–36	0%
Lidocaine						
Senat	2003	Intrafunic	70–300 mg	50	20–36	8%
Chen	2009	Intracardiac	200 mg	7	24–38	14.3%
Lopez-Cepero	2013	Intracardiac or intrathoracic	50–400 mg	50–400	Mean 22 (SD 2.3. Range not reported)	7.4%
Reeves	2019	Intrafetal, transabdominal	200–240 mg	75	Not reported	0%
		Intrafetal, transvaginal	200–240 mg	62		38.7%
Tolu	2021	Intracardiac	200 mg	80	21–27.5	5%
Reeves	2022	Intracardiac or intrathoracic	200–480 mg	338	24–32	2.1%
Sium	2022	Intracardiac	200 mg	16	20–28	0%

injected 0 to 3 days before the abortion procedure. Potassium chloride is administered incrementally until asystole is achieved.[52–55] One study compared the transabdominal to transcervical or transvaginal approach, although this was specifically in the context of fetal reduction earlier in pregnancy; the primary outcome was success rates of delivery in the setting of selective termination and multifetal reduction, so little data reviewed the success rates of the injections to induce asystole.[56] Of note, studies examining the injection location are mostly retrospective cohort studies, as the factors affecting choice of injection location often are not randomizable.

Dose

Studies have documented a wide variety of doses of potassium chloride to induce fetal asystole. For multifetal pregnancy reduction before 14 0/7 weeks of gestation, current guidelines recommend the use of potassium chloride 1–4 mEq (0.5–2 mL) of 2 mEq/mL, injected under ultrasound guidance to watch for asystole.[57] From 14 0/7 to 27 6/7 weeks of gestation, doses range from 2 to 80 mEq (1–40 mL) of 2 mEq/mL, but a dose of 6 to 20 mEq (3–10 mL) of 2 mEq/mL is most typically used for inducing fetal asystole.[48,49,52,54,55] Starting at 32 weeks of gestation, the literature supports doses of potassium chloride 10 to 20 mEq (5–10 mL) of 2 mEq/mL for selective fetal reduction.[57] One study found a significant correlation between dose and estimated fetal weight but not between dose and gestational duration, although the discordance between size and gestational duration in a fetus with anomalies or genetic diagnoses may have contributed.[54] Other studies have not found relationships between gestational duration with dose or have used standard dosing regardless of estimated fetal weight.[49,50]

Effectiveness

Potassium chloride has proven to be highly successful in inducing fetal asystole rapidly. Multiple studies have shown 100% success inducing asystole with the first injection.[46,52,54] One retrospective review of 239 cases documented asystole after the first injection in every case using intracardiac potassium chloride 6 to 10 mEq.[52] Another retrospective review found a 99.5% success rate, with 191 of 192 cases inducing asystole on first injection using intracardiac potassium chloride 3 to 40 mL.[54] One study of 158 cases comparing two intracardiac methods of potassium chloride injection (interventricular septal and intraventricular) found injection into the interventricular septum resulted in significantly lower median total doses (3 mL vs 5 mL, $p < 0.001$), significantly shorter median time to reach asystole (42 seconds vs 115 seconds, $p < 0.001$), and significantly shorter median total duration of the procedure (85 seconds vs 150 seconds, $p < 0.001$). Both methods achieved asystole in 100% of the cases on first injection; however, the study had a sample size of 158 patients.[55]

Intrafunic potassium chloride has had more varied results. Early studies did not document success rates, but later studies found failure of the first injection to vary from 0% to 13.3%.[48–51] These studies were smaller, with retrospective reviews documenting failure rates of 13% and 9% in 60 and 21 cases, respectively.[48,49] In one study, five of the eight failures were due to the inability to confirm or maintain intrafunic location, underscoring the increased technical difficulty of transabdominal intrafunic placement.[48] A recent study of intrafunic injection done intraoperatively during the procedural abortion via dilation and evacuation found 100% efficacy in 32 cases (95% CI 90.6%–100%). Their procedure involved extracting the umbilical cord through the cervix after cervical dilation was achieved and direct visualization of the umbilical vein; thus, identification of umbilical vein on ultrasound was not a factor.[51] No RCTs compare the efficacy of intrafunic to intracardiac injection.

Risks

Limited case reports have described intrauterine infection associated with intrafunic[58] and intracardiac[59] injections and extramural delivery.[48] Discomfort at the injection site can occur.[54] Specific to potassium chloride is the significant risk of cardiac toxicity if injected into the circulation of the pregnant individual. A published case report describes a cardiac arrest of the pregnant individual associated with fetal intracardiac injection of potassium chloride; advanced cardiac life support was initiated, with the patient cardioverted into sinus rhythm. The patient had a potassium chloride concentration of 3.9 mmol/L within 15 minutes of the arrest.[60] Hyperkalemia can induce cardiac arrhythmias at lower serum levels too. Confirming the potassium chloride injection site, therefore, is critical.

Challenges

Achieving intracardiac or intrafunic placement may be challenging to clinicians, particularly if they have less ultrasound-guided procedure training. No studies describe other intrafetal locations.

Lidocaine

Technique

Lidocaine is an antiarrhythmic anesthetic that inhibits sodium ion channels and inhibits nerve impulse initiation and conduction. Under ultrasound guidance a spinal needle is placed transabdominally in a fetal cardiac ventricle where aspiration of fetal blood will confirm correct placement.[61–63] Transvaginal intrafetal cardiac lidocaine injection to induce fetal asystole has also been described.[64]

Dose

The dose of lidocaine used to induce fetal asystole is variable. Most reports use lidocaine 200 mg (20 mL of 1% lidocaine or 10 mL 2% lidocaine).[35,62–64] If asystole was not achieved within several minutes, an additional 20 mL of 1% lidocaine was injected. Two studies used different dosages based on gestational duration, ranging from 70 to 300 mg (7–30 mL of 1% lidocaine) in one study and 50 to 400 mg (5–50 mL of 1% lidocaine) in another.[61,65] A third retrospective cohort analysis of patients undergoing transabdominal intracardiac lidocaine injections reported no significant difference in successful induction of fetal asystole between patients who received 200 to 240 mg ($n = 310$) and those who received 400 to 480 mg

($n = 27$; $p > 0.05$) for the first injection; a second injection was required to induce asystole in five fetuses.[63] Among singleton gestations, asystole was successfully achieved with a single injection in 99.1% of cases (95% CI 97.4%−99.8%), whether intracardiac (99.3%, 95% CI 97.5%−99.9%) or intrathoracic (97.8%, 95% CI 88.5%−99.9%).[63] One study recommended the use of 10 to 30 mL of 1% lidocaine (100−300 mg) for use in selective termination in the third trimester.[57] Of note, the doses in these studies were given in different intrafetal locations, that is, intracardiac, intrathoracic, and intrafunic.

Effectiveness

Lidocaine is effective in inducing fetal asystole, especially with a transabdominal intrathoracic or intracardiac placement. One retrospective cohort study found transabdominal intracardiac injection of lidocaine successful in 98.3% of cases, while intrathoracic was successful in 95.7%.[63] When administered transabdominally in other studies, rates of success of first injection have been reported as 92% to 100%.[35,61,62,64,65] Limited data report lower rates of success for transvaginal intrafetal administration (82% and 57% effective at 22 to 23 and 24 weeks of gestation or more, respectively), largely because most injections were not intrathoracic.[64] A beneficial aspect of lidocaine is its quick onset of action, such as potassium chloride, with asystole confirmed during the injection in most reported cases.[61−63]

Risks

A demonstrated risk of lidocaine injection is lidocaine toxicity, which can present with tinnitus[62,63] and vomiting.[62] Even if lidocaine accidentally were injected directly into the circulation of the pregnant individual, the doses used are well below dosing commonly used in anesthesia (approximately 2 mg/kg/h)[67] and well below the toxic levels of 7 mg/kg.[66] No publications report lidocaine injection−associated infections, although this is likely due to the small number of studies rather than any difference in risk from lidocaine injection compared with other agents.

Challenges

Achieving intracardiac or intrathoracic placement may be challenging to clinicians or those with less ultrasound-guided procedure training.[63] More data are needed to understand the need for intrathoracic or intracardiac placement vs placement in other intrafetal locations.

We recommend that clinicians identify the optimal pharmacologic agent to administer for a given clinical scenario based on factors such as availability of each agent; the time frame in which fetal asystole needs to be established; and clinicians' technical ability, preferences, and practice (Best Practice).

Potassium chloride, lidocaine, and digoxin are all acceptable pharmaceutical agents to induce fetal asystole before abortion. To establish asystole rapidly, we suggest using potassium chloride (via intracardiac or intrafunic injection) or lidocaine (via intracardiac or intrafunic injection) (GRADE 2C), although intrathoracic administration of lidocaine may be acceptable. We recommend potassium chloride not be used if intracardiac or intrafunic location cannot be achieved to avoid the risk of accidental administration to the pregnant individual and because insufficient data support its efficacy via other intrafetal locations (GRADE 1C).

When using digoxin, we recommend intrafetal administration (GRADE 1C), although intraamniotic administration may be acceptable depending on a clinician's technical ability and setting. Because digoxin may take several hours to induce asystole, an alternative agent should be considered in settings where fetal asystole must be confirmed rapidly.

Methods to induce fetal asystole at the time of procedural abortion.

If asystole is not induced before a procedural abortion, pharmacological or mechanical methods can be used as part of the procedural abortion. These methods may require cervical dilation, amniotomy, and accessing the umbilical cord external to the cervical os. They may prolong procedure time, which increases sedation requirements and may not result in asystole before uterine evacuation.

Umbilical transection techniques have been completed after dilation of the cervix during multifetal pregnancy reduction and selective termination endoscopic procedures.[28,56,68−71] After dividing the umbilical cord, the time to asystole ranges widely, from under 3 minutes to as much as 28 minutes.[51] A case series of 407 patients, 16 to 22 weeks of gestation, described umbilical cord transection as the first step of a procedural abortion via dilation and evacuation.[72] After the removal of natural osmotic cervical dilators (laminaria) and amniotomy, the fetal cord was brought to the external os by the suction cannula and transected. The mean time from cord transection to asystole was 3.3 minutes, with a range from less than 1 minute to 11 minutes. In a case series of 57 patients, Nippita et al. describe the time to asystole after intrafunic injection of potassium chloride at the time of procedural abortion via dilation and evacuation.[51] The use of potassium chloride resulted in asystole within 210 seconds for all cases except one.[51] The median time to asystole was 48 seconds (interquartile range 34−100 seconds). In one procedure, cord transection was done when asystole did not occur within 5 minutes of potassium chloride injection, and asystole occurred 28 minutes later.[51] If not using a pharmacologic agent to induce asystole and the clinician cannot transect the cord, procedural techniques can be used to induce asystole, such as removing the placenta first or decompressing the calvarium. When considering these methods, the benefit of avoiding preterm delivery of a viable fetus should be weighed against the risks of prolonged procedural time and the need for increased sedation.

2.5. Can techniques for inducing fetal asystole before abortion be used to induce fetal asystole for multifetal pregnancy reduction or selective termination?

While techniques to induce fetal asystole before abortion use many of the same pharmaceutical agents as approaches for multifetal pregnancy reduction or selective termination, recommendations for inducing fetal asystole cannot be applied universally for these indications.

Complicating factors such as chorionicity, amnionicity, and technical considerations such as accessibility will influence the approach for selective reduction or reduction of multifetal gestations.[73] Nondirective patient counseling that discusses the risks unique to multifetal gestation, as well as the option to continue or reduce the pregnancy, is also a key element of this care. Therefore, management of selective termination or multifetal pregnancy reduction is outside the scope of this document. Clinicians should reference clinical guidance specific to these topics.[74,75]

2.6. What are some implementation considerations that could affect whether to offer induction of fetal asystole before abortion?

Some clinicians operate within settings where they can induce fetal asystole but cannot provide the necessary subsequent procedures. For example, fetal asystole injections generally occur in outpatient settings. However, medication and procedural abortion after inducing fetal asystole sometimes are offered in a hospital, which may involve more complex management for patients with medical comorbidities. Due to a range of considerations, clinicians and patients may choose to induce fetal asystole in one clinical setting while anticipating the need to pursue abortion care in another setting. In this scenario, clinicians should be aware of the legal context and, if possible, discuss with the patient the need for prompt medical attention for delivery of the demised fetus. The legal and reimbursement landscapes surrounding this care are complex, and clinicians and institutions should be familiar with laws and requirements applicable in their setting.

3. Conclusions and recommendations

Please see Table 1 for a key to interpreting GRADE.

- Insufficient evidence exists to recommend routine induction of fetal asystole before a previable **medication abortion.**
- Insufficient evidence exists to recommend routine induction of fetal asystole before a previable **procedural abortion** because it has not been shown conclusively to improve the ease of procedure or reduce complications during dilation and evacuation.
- At periviable gestations and after fetal viability, induction of fetal asystole before abortion prevents the infrequent but serious occurrence of unanticipated expulsion of a fetus with cardiorespiratory activity (Best Practice). Defining viability is complicated as it represents a physiological continuum impacted by gestational duration along with multiple other individual clinical factors and circumstances; therefore, the exact gestational duration to offer fetal asystole will depend on the setting and clinical circumstances.
- If induction of fetal asystole before abortion is available, we recommend engaging in patient-centered counseling regarding the risks and benefits of induction of fetal asystole in the setting of each unique pregnancy scenario and the patient's beliefs and priorities (Best Practice).
- We recommend that clinicians identify the optimal pharmacologic agent to administer for a given clinical scenario based on factors such as availability of each agent; the time frame in which fetal asystole needs to be established; and clinicians' technical ability, preferences, and practice (Best Practice).
- Potassium chloride, lidocaine, and digoxin are all acceptable pharmaceutical agents to induce fetal asystole before abortion. To establish asystole rapidly, we suggest using potassium chloride (via intracardiac or intrafunic injection) or lidocaine (via intracardiac or intrafunic injection) (GRADE 2C), although intrathoracic administration of lidocaine may be acceptable.
- We recommend potassium chloride not be used if intracardiac or intrafunic location cannot be achieved to avoid the risk of accidental administration to the pregnant individual and because insufficient data support its efficacy via other intrafetal locations (GRADE 1C).
- When using digoxin, we recommend intrafetal administration (GRADE 1C), although intraamniotic administration of digoxin may be acceptable depending on a clinician's technical ability and setting. Because digoxin may take several hours to induce asystole, an alternative agent should be considered in settings where fetal asystole must be confirmed rapidly.

4. Recommendations for future research

- Clinical outcomes of inducing fetal asystole before medication or procedural abortion, including effects on length of procedure, hemorrhage risk, and blood loss.
- Examination of how inducing fetal asystole changes clinical outcomes and patient experience across gestational durations to help identify gestations at which it may be more strongly indicated.
- Better understanding of optimal route, dose, and timing for digoxin, potassium chloride, and lidocaine, as well as improved enumeration and understanding of the risks of each agent (e.g., extramural delivery, side effects).
- Patient needs, desires, and experiences surrounding induction of fetal asystole (e.g., the effect of induction of fetal asystole on pregnant patients' experience of pain; whether patients are interested in having the option for induction of asystole in one setting, even if they would have to then present elsewhere for further management).

5. Sources

A series of clinical questions were developed by the authors and reviewed by representatives from the Society of Family Planning's Clinical Affairs Committee. We searched the PubMed database to identify relevant articles published between January 2009 and September 2022. Search terms included, but were not limited to, feticide, feticidal, abortion, fetal asystole, termination, induced abortion, induction, demise, selective termination, pregnancy reduction, and multifetal pregnancy reduction. The

search was restricted to articles published in the English language. We also reviewed guidelines published by organizations or institutions, such as the Centers for Disease Control and Prevention, the American College of Obstetricians and Gynecologists, and the Society of Family Planning, as well as relevant product labels. We located additional studies by reviewing references of identified articles. When reliable research was not available, expert opinion from family planning and maternal-fetal medicine clinicians was used.

6. Intended audience

This Clinical Recommendation is intended for the Society of Family Planning and the Society for Maternal-Fetal Medicine members; family planning, maternal-fetal medicine, and reproductive health service clinicians; reproductive health researchers; consumers of family planning care; and policymakers. ■

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Planned Parenthood Federation of America endorses this document.

AUTHORSHIP

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REFERENCES

1. Diedrich J, Drey E; Society of Family Planning. Induction of fetal demise before abortion. Contraception 2010;81:462–73. https://doi.org/10.1016/j.contraception.2010.01.018.

2. American College of Obstetricians and Gynecologists. Abortion Policy n.d. ⟨https://www.acog.org/clinical-information/policy-and-position-statements/statements-of-policy/2022/abortion-policy⟩ (accessed November 16, 2023).

3. Jones RK, Kirstein M, Philbin J. Abortion incidence and service availability in the United States, 2020. Perspect Sex Reprod Health 2022;54:128–41. https://doi.org/10.1363/psrh.12215.

4. Kapp N, Lohr PA. Modern methods to induce abortion: safety, efficacy and choice. Best Pract Res Clin Obstet Gynaecol 2020;63:37–44. https://doi.org/10.1016/j.bpobgyn.2019.11.008.

5. Dragoman M., Paul M. . Incremental Expansion of Dilation and Evacuation (D&E) Provision From 24 to 26 Weeks. Later Abortion Initiative: Ibis Reproductive Health; 2023. (https://laterabortion.org/incremental-expansion-abortion-care). (accessed August 7, 2024).

6. Aberg A, Mitelman F, Cantz M, Gehler J. Cardiac puncture of fetus with Hurler's disease avoiding abortion of unaffected co-twin. Lancet 1978;2:990–1. https://doi.org/10.1016/s0140-6736(78)92550-3.

7. Abortion & Reproductive Rights Supreme Court Cases. Justia Law n.d. ⟨https://supreme.justia.com/cases-by-topic/abortion-reproductive-rights/⟩ (accessed November 16, 2023).

8. Sobel L., Ramaswamy A., Published A.S. Abortion at SCOTUS: Dobbs v. Jackson Women's Health - Table - 9823—02. KFF 2022. ⟨https://www.kff.org/report-section/abortion-at-scotus-dobbs-v-jackson-womens-health-table/⟩ (accessed November 16, 2023).

9. American College of Obstetricians and Gynecologists. More Than 75 Health Care Organizations Release Joint Statement in Opposition to Legislative Interference 2022. ⟨https://www.acog.org/news/news-releases/2022/07/more-than-75-health-care-organizations-release-joint-statement-in-opposition-to-legislative-interference⟩ (accessed July 2, 2024).

10. Gostin LO, Wetter S, Reingold RB. One year after Dobbs-Vast changes to the abortion legal landscape. JAMA Health Forum 2023;4:e233091. https://doi.org/10.1001/jamahealthforum.2023.3091.

11. American College of Obstetricians and Gynecologists. Understanding and Navigating Viability n.d. ⟨https://www.acog.org/advocacy/facts-are-important/understanding-and-navigating-viability⟩ (accessed November 16, 2023).

12. American College of Obstetricians and Gynecologists. Periviable birth. Obstetric Care Consensus No. 6. Obstet Gynecol 2017;130:e187–99.

13. Elimian A, Verma U, Tejani N. Effect of causing fetal cardiac asystole on second-trimester abortion. Obstet Gynecol 1999;94:139–41. https://doi.org/10.1016/s0029-7844(99)00273-2.

14. Srisomboon J, Pongpisuttinun S. Efficacy of intracervicovaginal misoprostol in second-trimester pregnancy termination: a comparison between live and dead fetuses. J Obstet Gynaecol Res 1998;24:1–5. https://doi.org/10.1111/j.1447-0756.1998.tb00044.x.

15. Silva LV, Cecatti JG, Pinto e Silva JL, Amaral E, Barini R. Feticide does not modify duration of labor induction in cases of medical termination of pregnancy. Fetal Diagn Ther 2008;23:192–7. https://doi.org/10.1159/000116740.

16. Şık A, Bilecan S, Kumbasar S, Akpak YK, Aba YA. Does feticide shorten termination duration in second trimester pregnancy terminations? Afr Health Sci 2019;19:1544–53. https://doi.org/10.4314/ahs.v19i1.28.

17. Ruano R, Dumez Y, Cabrol D, Dommergues M. Second- and third-trimester therapeutic terminations of pregnancy in cases with complete placenta previa–does feticide decrease postdelivery maternal hemorrhage? Fetal Diagn Ther 2004;19:475–8. https://doi.org/10.1159/000080157.

18. Jackson RA, Teplin VL, Drey EA, Thomas LJ, Darney PD. Digoxin to facilitate late second-trimester abortion: a randomized, masked, placebo-controlled trial. Obstet Gynecol 2001;97:471–6. https://doi.org/10.1016/s0029-7844(00)01148-0.

19. Lohr PA, Parsons JH, Taylor J, Morroni C. Outcomes of dilation and evacuation with and without feticide by intra-cardiac potassium chloride injection: a service evaluation. Contraception 2018;98:100–5. https://doi.org/10.1016/j.contraception.2018.04.010.

20. Denny CC, Baron MB, Lederle L, Drey EA, Kerns JL. Induction of fetal demise before pregnancy termination: practices of family planning providers. Contraception 2015;92:241–5. https://doi.org/10.1016/j.contraception.2015.05.002.

21. Hern WM. Laminaria, induced fetal demise and misoprostol in late abortion. Int J Gynaecol Obstet 2001;75:279–86. https://doi.org/10.1016/s0020-7292(01)00478-7.

22. McNamara B, Russo J, Chaiken S, Jacobson J, Kerns J. A qualitative study of digoxin injection before dilation and evacuation. Contraception 2018;97:515–9. https://doi.org/10.1016/j.contraception.2018.02.004.

23. Royal College of Obstetricians & Gynaecologists. RCOG Fetal Awareness Evidence Review, December 2022. Royal College of Obstetricians & Gynaecologists; 2009.

24. Norton ME, Cassidy A, Ralston SJ, Chatterjee D, Farmer D, Beasley AD, et al. Society for Maternal-Fetal Medicine Consult Series #59: the use of analgesia and anesthesia for maternal-fetal procedures. Contraception 2022;106:10–5. https://doi.org/10.1016/j.contraception.2021.10.003.

25. Lee SJ, Ralston HJP, Drey EA, Partridge JC, Rosen MA. Fetal pain: a systematic multidisciplinary review of the evidence. JAMA 2005;294:947–54. https://doi.org/10.1001/jama.294.8.947.

26. Davis KD, Bushnell MC, Iannetti GD, St Lawrence K, Coghill R. Evidence against pain specificity in the dorsal posterior insula. F1000Res 2015;4:362. https://doi.org/10.12688/f1000research.6833.1.

27. Verriotis M, Chang P, Fitzgerald M, Fabrizi L. The development of the nociceptive brain. Neuroscience 2016;338:207–19. https://doi.org/10.1016/j.neuroscience.2016.07.026.

28. Beksaç MS, Balci S, Ozlü T, Ozyüncü O. Selective feticide in dichorionic pregnancies with intracardiac blood aspiration: report of nine

cases. J Perinat Med 2009;37:85–6. https://doi.org/10.1515/JPM.2009.010.
29. Rodeck CH, Mibashan RS, Abramowicz J, Campbell S. Selective feticide of the affected twin by fetoscopic air embolism. Prenat Diagn 1982;2:189–94. https://doi.org/10.1002/pd.1970020308.
30. White KO, Nucatola DL, Westhoff C. Intrafetal compared with intra-amniotic digoxin before dilation and evacuation: a randomized controlled trial. Obstet Gynecol 2016;128:1071–6. https://doi.org/10.1097/AOG.0000000000001671.
31. Dean G, Colarossi L, Lunde B, Jacobs AR, Porsch LM, Paul ME. Safety of digoxin for fetal demise before second-trimester abortion by dilation and evacuation. Contraception 2012;85:144–9. https://doi.org/10.1016/j.contraception.2011.05.016.
32. Molaei M, Jones HE, Weiselberg T, McManama M, Bassell J, Westhoff CL. Effectiveness and safety of digoxin to induce fetal demise prior to second-trimester abortion. Contraception 2008;77:223–5. https://doi.org/10.1016/j.contraception.2007.10.011.
33. Drey EA, Thomas LJ, Benowitz NL, Goldschlager N, Darney PD. Safety of intra-amniotic digoxin administration before late second-trimester abortion by dilation and evacuation. Am J Obstet Gynecol 2000;182:1063–6. https://doi.org/10.1067/mob.2000.105438.
34. Hern WM, Zen C, Ferguson KA, Hart V, Haseman MV. Outpatient abortion for fetal anomaly and fetal death from 15-34 menstrual weeks' gestation: techniques and clinical management. Obstet Gynecol 1993;81:301–6.
35. Sium AF, Tufa TH, Grentzer JM, Prager S. Effectiveness of intra-cardiac lidocaine and intra-amniotic digoxin at inducing fetal demise before second trimester abortion past 20 weeks at a tertiary Hospital in Ethiopia: a retrospective review. Contracept X 2022;4:100082. https://doi.org/10.1016/j.conx.2022.100082.
36. Tocce K, Sheeder JL, Edwards LJ, Teal SB. Feasibility, effectiveness and safety of transvaginal digoxin administration prior to dilation and evacuation. Contraception 2013;88:706–11. https://doi.org/10.1016/j.contraception.2013.08.005.
37. Gariepy AM, Chen BA, Hohmann HL, Achilles SL, Russo JA, Creinin MD. Transvaginal administration of intraamniotic digoxin prior to dilation and evacuation. Contraception 2013;87:76–80. https://doi.org/10.1016/j.contraception.2012.07.019.
38. Nucatola D, Roth N, Gatter M. A randomized pilot study on the effectiveness and side-effect profiles of two doses of digoxin as fetocide when administered intraamniotically or intrafetally prior to second-trimester surgical abortion. Contraception 2010;81:67–74. https://doi.org/10.1016/j.contraception.2009.08.014.
39. Tufa TH, Lavelanet AF, Belay L, Seboka B, Bell J. Feasibility of intra-amniotic digoxin administration by obstetrics and gynecology trainees to induce fetal demise prior to medical abortion beyond 20 weeks. BMJ Sex Reprod Health 2020;46:308–12. https://doi.org/10.1136/bmjsrh-2019-200396.
40. Sharvit M, Klein Z, Silber M, Pomeranz M, Agizim R, Schonman R, et al. Intra-amniotic digoxin for feticide between 21 and 30 weeks of gestation: a prospective study. BJOG 2019;126:885–9. https://doi.org/10.1111/1471-0528.15640.
41. Steward R, Melamed A, Kim R, Nucatola D, Gatter M. Infection and extramural delivery with use of digoxin as a feticidal agent. Contraception 2012;85:150–4. https://doi.org/10.1016/j.contraception.2011.01.005.
42. Westendorp AK, Miny P, Holzgreve W, De Wilde R, Aydinli K. Selective fetocide by direct intracardiac injection of isotonic potassium chloride. Arch Gynecol Obstet 1988;244:59–62. https://doi.org/10.1007/BF00931404.
43. Evans MI, Dommergues M, Wapner RJ, Lynch L, Dumez Y, Goldberg JD, et al. Efficacy of transabdominal multifetal pregnancy reduction: collaborative experience among the world's largest centers. Obstet Gynecol 1993;82:61–6.
44. Evans MI, Goldberg JD, Dommergues M, Wapner RJ, Lynch L, Dock BS, et al. Efficacy of second-trimester selective termination for fetal abnormalities: international collaborative experience among the world's largest centers. Am J Obstet Gynecol 1994;171:90–4. https://doi.org/10.1016/s0002-9378(94)70083-4.
45. Evans MI, Dommergues M, Wapner RJ, Goldberg JD, Lynch L, Zador IE, et al. International, collaborative experience of 1789 patients having multifetal pregnancy reduction: a plateauing of risks and outcomes. J Soc Gynecol Investig 1996;3:23–6. https://doi.org/10.1016/1071-5576(95)00037-2.
46. Berkowitz RL, Stone JL, Eddleman KA. One hundred consecutive cases of selective termination of an abnormal fetus in a multifetal gestation. Obstet Gynecol 1997;90:606–10. https://doi.org/10.1016/s0029-7844(97)00312-8.
47. Evans MI, Goldberg JD, Horenstein J, Wapner RJ, Ayoub MA, Stone J, et al. Selective termination for structural, chromosomal, and mendelian anomalies: international experience. Am J Obstet Gynecol 1999;181:893–7. https://doi.org/10.1016/s0002-9378(99)70321-2.
48. Gill P, Cyr D, Afrakhtah M, Mack L, Easterling T. Induction of fetal demise in advanced pregnancy terminations: report on a funic potassium chloride protocol. Fetal Diagn Ther 1994;9:278–82. https://doi.org/10.1159/000263948.
49. Bhide A, Sairam S, Hollis B, Thilaganathan B. Comparison of feticide carried out by cordocentesis versus cardiac puncture. Ultrasound Obstet Gynecol 2002;20:230–2. https://doi.org/10.1046/j.1469-0705.2002.00797.x.
50. Senat MV, Fischer C, Ville Y. Funipuncture for fetocide in late termination of pregnancy. Prenat Diagn 2002;22:354–6. https://doi.org/10.1002/pd.290.
51. Nippita S, Carranza ASO, Paul ME. Funic potassium chloride injection during intact dilation and evacuation. Contraception 2021;104:275–7. https://doi.org/10.1016/j.contraception.2021.03.029.
52. Pasquini L, Pontello V, Kumar S. Intracardiac injection of potassium chloride as method for feticide: experience from a single UK tertiary centre. BJOG 2008;115:528–31. https://doi.org/10.1111/j.1471-0528.2007.01639.x.
53. Chen C-H, Chen T-H, Kuo S-J, Chen C-D, Yang Y-S, Chen M. Late termination of pregnancy: experience from East Asian population and report of a novel technique for feticide. J Med Ultrasound 2009;17:193–9.
54. Sfakianaki AK, Davis KJ, Copel JA, Stanwood NL, Lipkind HS. Potassium chloride-induced fetal demise: a retrospective cohort study of efficacy and safety. J Ultrasound Med 2014;33:337–41. https://doi.org/10.7863/ultra.33.2.337.
55. Süzen Çaypınar S, Oğlak SC, Polat İ, Kurt Bilirer K, Sezer S, Gedik Özköse Z, et al. A new and more effective feticide technique in late termination of pregnancy: potassium chloride injection into the interventricular septum of the fetal heart. Arch Gynecol Obstet 2023;307:779–87. https://doi.org/10.1007/s00404-022-06795-8.
56. Evans MI, Dommergues M, Timor-Tritsch I, Zador IE, Wapner RJ, Lynch L, et al. Transabdominal versus transcervical and transvaginal multifetal pregnancy reduction: international collaborative experience of more than one thousand cases. Am J Obstet Gynecol 1994;170:902–9. https://doi.org/10.1016/s0002-9378(94)70306-x.
57. Beriwal S, Impey L, Ioannou C. Multifetal pregnancy reduction and selective termination. Obstet Gynaecol 2020;22:284–92. https://doi.org/10.1111/tog.12690.
58. Li Kim Mui SV, Chitrit Y, Boulanger MC, Maisonneuve L, Choudat L, de Bièvre P. Sepsis due to Clostridium perfringens after pregnancy termination with feticide by cordocentesis: a case report. Fetal Diagn Ther 2002;17:124–6. https://doi.org/10.1159/000048022.
59. Lipitz S, Shalev E, Meizner I, Yagel S, Weinraub Z, Jaffa A, et al. Late selective termination of fetal abnormalities in twin pregnancies: a multicentre report. Br J Obstet Gynaecol 1996;103:1212–6. https://doi.org/10.1111/j.1471-0528.1996.tb09631.x.
60. Coke GA, Baschat AA, Mighty HE, Malinow AM. Maternal cardiac arrest associated with attempted fetal injection of potassium chloride. Int J Obstet Anesth 2004;13:287–90. https://doi.org/10.1016/j.ijoa.2004.04.009.
61. López-Cepero R, Lynch L, de la Vega A. Effectiveness and safety of lidocaine in the induction of fetal cardiac asystole for second trimester pregnany termination. Bol Asoc Med P R 2013;105:14–7.
62. Tolu LB, Tufa TH, Abas F, Kahn C, MacAfee L, Prager S, et al. Intra-cardiac

lidocaine administration to induce fetal demise before late second-trimester abortion: Retrospective review. Int J Gynaecol Obstet 2021;153:125–9. https://doi.org/10.1002/ijgo.13419.
63. Reeves MF, Goldfarb CN, Rubin SL, Kuperstock JL, DiBianco L, Picciotto A. Transabdominal lidocaine to induce fetal demise: a cohort study. BMJ Sex Reprod Health 2022;48:275–80. https://doi.org/10.1136/bmjsrh-2021-201350.
64. Reeves MJ, Rubin SL, Goldfarb CN. Intrafetal injection of lidocaine to induce fetal demise. Contraception 2019;99:319. https://doi.org/10.1016/j.contraception.2019.03.014.
65. Senat MV, Fischer C, Bernard JP, Ville Y. The use of lidocaine for fetocide in late termination of pregnancy. BJOG 2003;110:296–300.
66. Torp K.D., Metheny E., Simon L.V. Lidocaine Toxicity. StatPearls, Treasure Island (FL): StatPearls Publishing; 2023.
67. Masic D, Liang E, Long C, Sterk EJ, Barbas B, Rech MA. Intravenous lidocaine for acute pain: a systematic review. Pharmacotherapy 2018;38:1250–9. https://doi.org/10.1002/phar.2189.
68. Ilagan JG, Wilson RD, Bebbington M, Johnson MP, Hedrick HL, Liechty KW, et al. Pregnancy outcomes following bipolar umbilical cord cauterization for selective termination in complicated monochorionic multiple gestations. Fetal Diagn Ther 2008;23:153–8. https://doi.org/10.1159/000111598.
69. Dommergues M, Nisand I, Mandelbrot L, Isfer E, Radunovic N, Dumez Y. Embryo reduction in multifetal pregnancies after infertility therapy: obstetrical risks and perinatal benefits are related to operative strategy. Fertil Steril 1991;55:805–11. https://doi.org/10.1016/s0015-0282(16)54252-6.
70. Boulot P, Hedon B, Pelliccia G, Lefort G, Deschamps F, Arnal F, et al. Multifetal pregnancy reduction: a consecutive series of 61 cases. Br J Obstet Gynaecol 1993;100:63–8. https://doi.org/10.1111/j.1471-0528.1993.tb12953.x.
71. Davis G, Liu DT. Mid-trimester abortion. Lancet 1972;2:1026. https://doi.org/10.1016/s0140-6736(72)92436-1.
72. Tocce K, Leach KK, Sheeder JL, Nielson K, Teal SB. Umbilical cord transection to induce fetal demise prior to second-trimester D&E abortion. Contraception 2013;88:712–6. https://doi.org/10.1016/j.contraception.2013.08.001.
73. Wimalasundera RC. Selective reduction and termination of multiple pregnancies. Semin Fetal Neonatal Med 2010;15:327–35. https://doi.org/10.1016/j.siny.2010.08.002.
74. American College of Obstetricians and Gynecologists. Committee Opinion No. 719: multifetal pregnancy reduction. Obstet Gynecol 2017;130:e158–63. https://doi.org/10.1097/AOG.0000000000002302.
75. American College of Obstetricians and Gynecologists. Multifetal gestations: twin, triplet, and higher-order multifetal pregnancies: ACOG Practice Bulletin, Number 231. Obstet Gynecol 2021;137:e145–62. https://doi.org/10.1097/AOG.0000000000004397.